JUL 20 1935

Vol. 6 JULY, 1935 No. 5

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PUBLISHED BI-MONTHLY

OFFICIAL ORGAN OF
THE SOCIETY FOR THE STUDY OF ASTHMA AND ALLIED CONDITIONS
THE ASSOCIATION FOR THE STUDY OF ALLERGY

PUBLISHED BY THE C. V. MOSBY COMPANY, 3523 PINE BOULEVARD
ST. LOUIS, U. S. A.

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The Journal of Allergy

CONTENTS FOR JULY, 1935

Original Articles

Inhalation of Epinephrine for the Relief of Asthmatic Symptoms. James B. Graeser, M.D., and Albert H. Rowe, M.D., Oakland, Calif. ---- 415

Food Idiosyncrasy as a Factor in the Digestive Leucocyte Response. Warren T. Vaughan, M.D., Richmond, Va. ---- 421

Oral Desensitization to Common Foods. Beatrice M. Kesten, M.D., Irene Waters, and J. Gardner Hopkins, M.D., New York, N. Y. ---- 431

Studies of Specificity in Multiple Hypersensitiveness by Quantitative Titration and Absorption of Reagins. Joseph Harkavy, M.D., and Ernst Witebsky, M.D., New York, N. Y. ---- 437

Practical Procedures in the Investigation of Certain Allergic Dermatoses. Marion B. Sulzberger, M.D., and Adolph Rostenberg, Jr., M.D., New York, N. Y. ---- 448

The Patch Test for Gold Hypersensitivity. M. R. Lichtenstein, M.D., Chicago, Ill. ---- 460

The Use of House Dust Oil and Thrasher Dust Oil in Contact Dermatitis. C. Malone Stroud, M.D., St. Louis, Mo. ---- 464

Psychogenic Urticaria. William C. Menninger, M.D., Topeka, Kan., and Jarold E. Kemp, M.D., Chicago, Ill. ---- 467

Dermatitis from Proprietary Hair Tonic. Herman Goodman, B.S., M.D., New York, N. Y. ---- 474

Drinking Water as a Cause of Eczema. L. O. Dutton, M.D., El Paso, Texas ---- 477

Studies in Atmospheric Pollen of San Francisco. William C. Deamer, M.D., San Francisco, and H. E. McMinn, M.A., Oakland, Calif. With the Technical Assistance of Bernadette Tilden and Elsa Brumlop ---- 480

A Botanical Survey of Northwestern California. Albert H. Rowe, M.D., Oakland, Calif., and J. Wendell Howe, M.A., Arcata, Calif. ---- 494

Death From Ten Grains of Aspirin. Nathan Francis, M.D., Oliver T. Ghent, M.D., and Stearns S. Bullen, M.D., Rochester, N. Y. ---- 504

A New Method for Covering Pillows. Gerald C. Grout, M.D., Dayton, Ohio ---- 507

Department of Reviews and Abstracts

Selected Abstracts ---- 509

Book Review ---- 516

The Journal of Allergy

VOL. 6 JULY, 1935 No. 5

Original Articles

INHALATION OF EPINEPHRINE FOR THE RELIEF OF ASTHMATIC SYMPTOMS*

JAMES B. GRAESER, M.D., AND ALBERT H. ROWE, M.D.
OAKLAND, CALIF.

ALTHOUGH epinephrine given hypodermically is the drug *par excellence* for relief of asthmatic symptoms, scant attention has been paid to the possibility of its administration by inhalation. This is surprising in view of the fact that the principle of inhalation has long been utilized in such widely used asthma remedies as the various stramonium powders and cigarettes, Tucker's spray, and other proprietary nostrums. The literature, however, reveals but few references on the subject of inhalation of epinephrine.

Bray in his book, *Recent Advances in Allergy*[1] casually mentions an apparatus called the Apneu inhalator, which utilizes compressed oxygen to spray epinephrine and stramonium into the air breathed. This apparatus, however, is apparently quite cumbersome, and Bray expresses little enthusiasm for its use. In contrast to his attitude is Camps' report,[2] describing several cases in which satisfactory relief of symptoms was obtained.

The present investigation was undertaken in an attempt to perfect a simplified method for the administration of epinephrine by inhalation. The 1:100 epinephrine solution nebulized by common atomizers gave inconclusive and negative results in our first trials. It seemed probable that our lack of success was due to the inability of the patient to inhale sufficient amounts of a solution of this concentration. We secured, therefore, through the courtesy of Parke, Davis and Company, a specially prepared 1:100 solution.

Patients having recurrent mild or moderately severe symptoms were selected from our private practice and charity clinic for the initial trials. In each case some routine form of medication had been established for relief of symptoms; epinephrine hypodermically, ephedrine, Asthmador

*Read before the Joint Meeting of The Society for the Study of Asthma and Allied Conditions and The Association for the Study of Allergy, Atlantic City, N. J., June 10 and 11, 1935.

or a kindred stramonium preparation, Tucker's spray, or other nostrum. In each instance the routine had been followed sufficiently long to permit evaluation of a new method. To date, a total of 40 patients have used the 1:100 solution nebulized by the atomizer later described.

For nebulizing the 1:100 epinephrine, various hand atomizers were first tried, but several difficulties soon disclosed the inadequacy of most of the available types. Several patients using one particular type delivering a coarse uneven spray complained of severe epigastric pain after inhalation. One other patient, while holding an atomizer in the mouth accidentally tipped it forward, allowing some of the solution to spill. This was swallowed and caused epigastric discomfort lasting several hours. In view of the latter experience it seemed probable that the aforementioned patients had likewise swallowed some of the solution, for the coarser sprays allowed large amounts of the epinephrine to drop into the mouth without being inhaled. For this reason, all patients using these instruments were advised to rinse their mouths with water immediately after spraying the epinephrine solution into the mouth. This precaution avoided further difficulty of this type. Patients using the less efficient atomizers complained also of an annoying dryness of the throat and mouth. Another objectionable feature was noted with atomizers having metal parts in contact with the epinephrine solution. In these the clear solution slowly changed to a dark brown color, a phenomenon associated with inactivation of the epinephrine.

From these experiences it was apparent that the ideal atomizer for this purpose should be constructed of glass, deliver an even vaporlike spray, and function when only small amounts of solution were present. With the cooperation of a local glass blower, such an atomizer was constructed by utilizing the same nebulizing mechanism as in the common all-glass atomizers, but modifying the apertures and chamber so that a uniformly fine spray was created. The chamber was also designed to produce maximum nebulization when but five or six drops of the solution were present.

The patients were instructed to place the nozzle of the atomizer just within the open mouth and to inhale deeply while creating a spray. The amount of inhalation varied for each patient, and depended not only on the severity of the symptoms, but also on the manner in which the atomizer was manipulated, i.e., the vigor with which the bulb was compressed, the correlation of inhalation with bulb compression, etc. Several patients noted, as a criterion of dosage, that they must inhale until cough occurred before relief was obtained. With the individual patient this, too, varied from one time to another. Since dosage could not be measured directly, as with hypodermic administration, the patients had to learn by experience to estimate dosage by the number of inhalations, as well as by the number of times of compression of the bulb. Until in-

dividual requirements were ascertained, the patient was advised to proceed slowly, allowing one to two minutes to elapse between several deep inhalations.

Inhalation of the 1:100 epinephrine vapor rarely causes any of the side effects, such as nervousness and tachycardia, which often follow epinephrine given subcutaneously. In fact, several patients so susceptible to these disturbances that doses as small as three or four minims caused discomfort were able to use the inhalation method with excellent relief of symptoms and minimal to none of the side effects. Moderate dryness of the throat occurs in about 30 per cent of the cases and varies with the different patients. This is mitigated somewhat by rinsing the mouth with water immediately following inhalation. Certain types of the common atomizers first used in our investigation caused an extreme sensation of dryness, and in one case persistent hoarseness to such a degree that the procedure had to be abandoned. With the improved atomizers such symptoms have never occurred with sufficient severity to necessitate discontinuance of inhalation.

One further aspect of this procedure should be explained to patients using the spray. In instances where relief of the paroxysm is followed by cough and expectoration of mucus, patients will frequently notice a bright pink color tinging the expelled secretion. Its resemblance to blood is, of course, alarming, but is to be explained by some chemical change taking place in the epinephrine. A less vivid but similar change may occur in the solution left in the atomizers.

The results obtained with inhalation of the 1:100 epinephrine solution have been uniformly successful. In most instances the physiologic effect occurred more rapidly than with hypodermic injection of the 1:1000 solution. Rarely is it any slower. So satisfactory have been the results that we feel the inhalation procedure may well supplant the use of epinephrine hypodermically in many instances at least. Furthermore its superiority to numerous proprietary remedies administered by inhalation has been amply demonstrated by our experiences. We have not as yet used the procedure in a case of status asthmaticus in which epinephrine given hypodermically has lost its effectiveness; so we are unable to state what results would be obtained in these instances.

COMMENT

Aside from the practical result of obtaining relief of asthmatic symptoms by the inhalation of epinephrine, there are several interesting considerations suggested by these experiments. On undertaking the investigation, we believed that by instilling a vapor of epinephrine into the lungs, absorption into the blood stream would occur, and the physiologic effects would take place as in subcutaneous injection. The rapidity of the effect and the infrequency of tachycardia, nervousness and other symptoms often occurring after injections of epinephrine suggested, however, that the results may be due to direct action on the bronchial mucosa. The

action might be compared to the topical application of epinephrine and ephedrine compounds on the swollen membrane of the allergic nasal mucosa. It is probable that the inhalation of the vaporlike spray distributes the epinephrine through the entire lung. Experiments in other fields verify the possibility of such a dissemination of inhaled spray or dusts throughout the bronchial tree. It has been shown for instance in experiments in mice inhaling bacteria laden sprays that the organisms may be recovered from all parts of the lungs if autopsy is performed soon after inhalation.[3] Likewise opaque dusts such as bismuth subcarbonate, when sprayed into the trachea of cats[4] or inspired into the lungs of dogs through a tracheal cannula,[5] will be distributed throughout the bronchial tree, as disclosed by roentgenograms.

We are interested in the further question of whether some patients whose symptoms are not yet controlled by specific allergic therapy, might mitigate the severity of their paroxysms by "prophylactic" inhalation of epinephrine. This has been suggested by our experience with several such patients who, shortly after beginning the use of this procedure, gradually diminished the necessity of its frequent use until finally one to two routine daily inhalations in symptom-free periods seemed to forestall the more severe paroxysms. A marked decrease in mucus coughed up during the day was associated with this change in their symptoms.

As yet our experience with the procedure described herein covers but several months, and in the history of these chronic sufferers such time is insufficient to evaluate entirely all aspects of the method. As one might expect, the enthusiasm of the patient who has found a convenient and effective means of symptomatic relief may tend to overshadow the more fundamental specific allergic therapy being carried out with the hope of eventually effecting a cure. This attitude should be forestalled by necessary explanation. It should be stressed, always, that epinephrine administration either hypodermically or by inhalation gives symptomatic relief only and cannot supersede study and treatment from an allergic point of view.

CONCLUSION

The inhalation of 1:100 epinephrine solution has been found to give satisfactory symptomatic relief of asthma in 40 patients having mild to moderate paroxysms. For administration, an atomizer delivering a vaporlike spray must be used. This procedure avoids the discomfort and inconvenience of hypodermic injection. It is rarely accompanied by any of the circulatory symptoms commonly following epinephrine administered hypodermically.

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5. Unpublished experiments of one of the authors (J. B. G.).

DISCUSSION ON "INHALATION OF EPINEPHRINE FOR THE RELIEF OF ASTHMATIC SYMPTOMS," BY DRS. GRAESER AND ROWE

DR. M. MURRAY PESHKIN, New York.—To my mind, Dr. Rowe has introduced a most useful apparatus from the standpoint of controlling asthmatic attacks. As a matter of fact, it will eventually prove a boon to allergists. In New York City and the Metropolitan area for the past eight years, we have been plagued with the commercial apparatus referred to by Dr. Rowe. Many ridiculous claims have emanated from this commercial source. I have seen a number of patients who have been obliged to resort to frequent hypodermic administration of epinephrine, change to the inhalation of the epinephrine mixture supplied with the commercial apparatus. Some of these patients obtain sufficient relief and seemed satisfied to the extent that they have unfortunately and unwisely discarded all rational medical treatment. At one time this commercial concern had advised its machine users to keep away from all doctors and remain orthodox to their instrument. I have been working with a similar type of instrument for several years but without much success, probably because I used only a 1:1,000 solution of epinephrine.

Absorption of a proper epinephrine solution by the mucous membranes of the nose and throat undoubtedly will relieve wheezing spells and mild asthmatic attacks. The injection of epinephrine will still be required for the relief of sharp attacks of asthma. With the increasing use of this apparatus I believe allergists will learn that it will encourage their patients to adhere patiently to the hyposensitization treatment which often extends over a period of one or more years.

I, for one, am extremely grateful to Dr. Rowe for making it possible to prescribe ethically this apparatus at a reasonable cost to the patient who needs it.

DR. S. J. PARLATO, BUFFALO.—I would like to ask Dr. Rowe how he accounts for the adrenalin solution getting by the protective mechanism in the larynx. We all know the introduction of a fine vapor in the larynx will cause a spasm of coughing. Has he noticed any secondary reactions from the use of adrenalin on the mucosa?

DR. GRAFTON TYLER BROWN, Washington, D. C.—I think we have all understood that the continued internasal application of epinephrine is inadvisable because it produces a secondary vasomotor reaction of the mucous membrane. If this occurs generally throughout the bronchial mucous membrane, it might leave us with a condition that is worse than we started with. I would like to ask Dr. Rowe if he has any comment on this point.

DR. ROWE.—Dr. Graeser and I are confident that the inhalation of 1:100 epinephrine solution will supplant in many instances the hypodermic administration of this drug. We thank Dr. Peshkin especially for his approval of our results. The effectiveness of this therapy is already being commercialized by a firm in the Northwest, and another German concern. With the simple atomizer we have described and the 1:100 epinephrine solution, the relief offered will be available for the patients of all physicians at a reasonable cost, and will discourage such commercialization. The possible relief obtained is greater than that resulting from the use of such nostrums as Tucker's Spray and the va-

rious stramonium powders. If the widespread use of these nostrums can be discouraged, the introduction of the 1:100 epinephrine will be justified.

In the last month we have developed a small motor driven pump for use with patients too ill or distressed to compress the rubber bulb, and with children unable to cooperate with the simple atomizer. The pump is attached to the atomizer by means of a rubber tube, and the atomizer itself is fitted into a metal mask designed to conform to the configuration of the face, over the nose and mouth. The vapor is then inhaled from the mask. This device can be manufactured for a small price compared with that charged for a more elaborate, though no more effective German machine used for similar therapy.

Parke, Davis and Company have cooperated with us in the experimental work with 1:100 epinephrine, and will soon distribute it for general use. Other commercial houses undoubtedly will do likewise and suitable atomizers which deliver a vapor will be available generally. The atomizers I have demonstrated, as well as the motor apparatus, may be obtained from the Peralta Hospital, Oakland, California.

FOOD IDIOSYNCRASY AS A FACTOR IN THE DIGESTIVE LEUCOCYTE RESPONSE*

WARREN T. VAUGHAN, M.D.
RICHMOND, VA.

THAT a systemic leucocytosis accompanies the process of alimentary digestion, is an observation which has been generally accepted and has remained unquestioned until the studies of Garrey and Butler,[1] who in 1932 concluded that what was formerly considered a leucocytosis resultant on digestion is actually one accompanying change in posture. The fasting patient, subject to study, has usually been in a state of recumbency through the night. With the administration of the test meal he assumes an erect or semierect posture. Garrey and Butler found that this change in posture alone, without feeding, produced an increase in the leucocyte count. Feeding without change of posture produced no noteworthy leucocytosis. They concluded that the existence of a digestive leucocytosis was doubtful. Raisky[2] of Germany reached similar conclusions later in the same year. On the contrary, Lawrence, Stephens and Jones[3] a year later concluded, from their studies, that a digestion leucocytosis of mild degree actually does exist.

The present communication represents a further study of this problem in which reliable investigators have presented diverse conclusions. Our attention has been centered on a factor which, while it has not received previous consideration, will be shown to be of sufficient importance to color any large series of investigations of the question.

Our own interest in the leucocytic response to digestion may be said to have begun in 1920 when Widal, Abrami and Iancovesco[4] first proposed the so-called colloidoclastic test for liver function. The test consisted, briefly, of the administration of 200 gm. of milk to the fasting subject. A consequent digestive leucocytosis was regarded as negative, while a leucopenia was interpreted as evidence of deranged liver function. In attempting to apply this test for hepatic function I, along with many others, concluded that it was not reliable, but I did observe that a number of patients giving positive colloidoclastic reactions were allergic to milk. This suggested the possibility that the ingestion of any food for which a person has an idiosyncrasy might be followed by a leucopenic response.

In 1932 an opportunity arose to make a very carefully controlled study of the leucocyte response to food ingestion in an allergic patient sensi-

*Read before a meeting of the Association of American Physicians, Atlantic City, May 7, 1935.

tive to a large number of foods, who, by virtue of previous four years of careful control, knew very precisely what foods caused allergic symptoms.[5] She was tested with sixteen foods, eleven of which were known to produce symptoms of greater or less severity. Counts were made fasting, and again ninety minutes after the ingestion of the test food. All eleven of the allergenic foods caused a leucocytic drop in the peripheral blood, of varying degree. None of the five to which she was not sensitive caused a drop, there resulting instead some degree of leucocytosis.

This preliminary study having indicated that food idiosyncrasy may produce a digestion leucopenia, a study was next undertaken to determine the leucocyte response to food ingestion in allergic persons. The first study comprised 191 leucopenic indices in about sixty patients. Most of the tests were made with the staples, wheat, egg, and milk, although a number of other foods were tested. Assuming that the allergic reaction to ingested foods consists of a leucocytic fall, we found on parallel studies of the leucopenic response and the positive skin reaction, that the two agreed in 62 per cent of the tests.[6] In the remaining 38 per cent the tests disagreed. In the latter the skin test was positive while the blood test was negative, or vice versa. Individuals in this group then experimented with the eating of those foods concerning which there was question. Some developed symptoms in confirmation of the positive skin reaction while others confirmed the leucopenic response. Briefly, the positive or negative leucopenic response was found to correspond with actual evidence of idiosyncrasy on food trial, in 70 per cent of cases.

Confirmatory evidence that the ingestion of foods against which one has experienced an idiosyncrasy is likely to be followed by a digestion leucopenia having been thus obtained, the investigation has been continued in a study of the digestive leucocyte response in individuals with known idiosyncrasy. Charts 1 to 10 bring out some most interesting observations.

The technic of the study was as follows: The patient reported to the office, fasting, and two white counts were made at ten-minute intervals. The patient then ate the food to be tested, after which serial white counts were performed at half-hour intervals for four hours. The same pipette and counting chamber were used throughout each test. During the period of study the patient sat around the office with no particular change of posture other than that of walking a few steps to the laboratory for each blood test, thereby obviating in great measure the criticism brought out by Garrey and Butler. In the charts the vertical lines in the "fasting" column indicate, for each patient, the ten-minute fasting range in the white count. The mean of the two

fasting counts was taken as zero. Postprandial rises or falls from this fasting zero level were charted and the curves plotted accordingly.

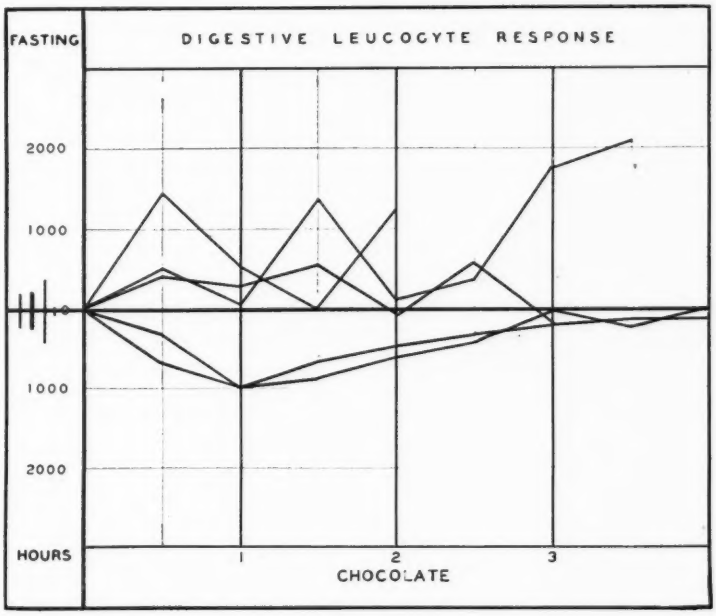

Chart 1.

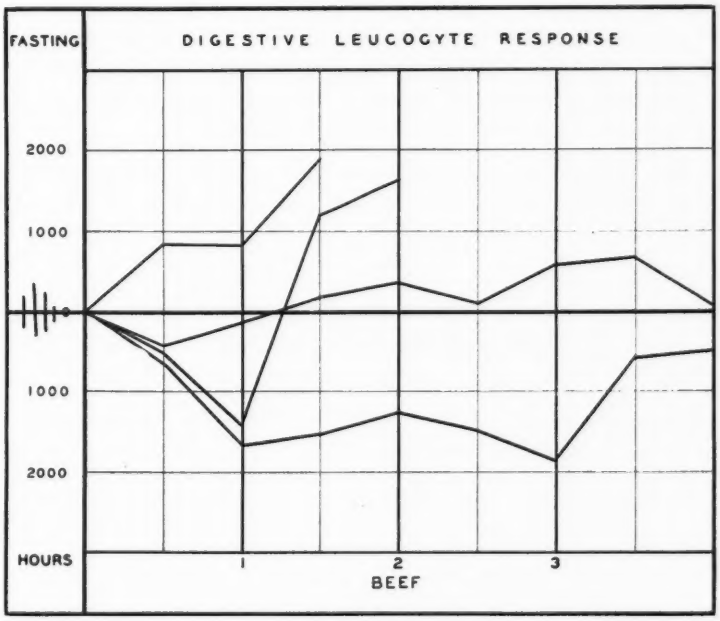

Chart 2.

The chart for chocolate represents a characteristic response. Three persons with no idiosyncrasy thereto reacted with curves practically

completely above the fasting level. Two persons who had experienced idiosyncrasy to chocolate, one in the form of dermatitis and the other colitis, showed a typical leucopenic response.

Four persons were tested with beef, two with idiosyncrasy and two without. The first without idiosyncrasy responded with a prompt leucocyte increase of nearly 2,000 at the end of ninety minutes. The second, after a slight preliminary drop, showed a moderate increase throughout. The third, sensitive to beef, displayed a rapid drop within an hour. At the end of this time she was severely nauseated, vomited six times, and at the end of an hour and a half the white count had risen to 1,300 above the fasting line, and continued up. She

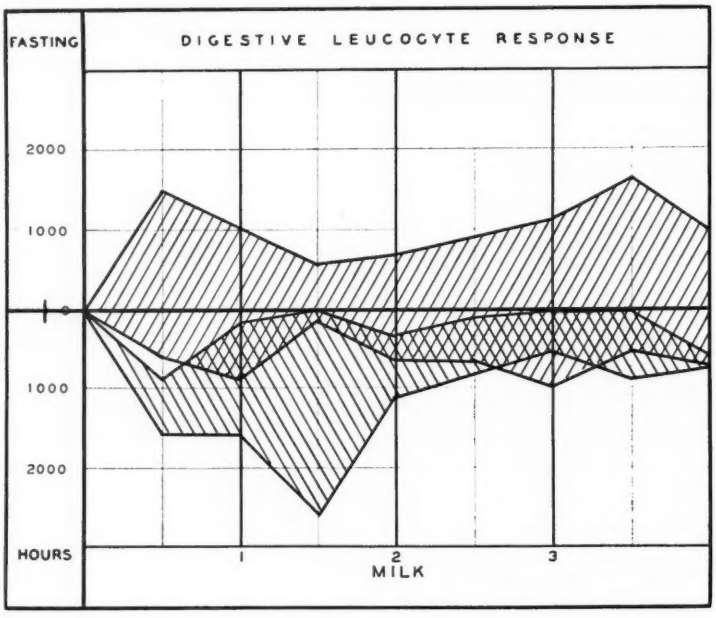

Chart 3.

was so sick at the end of two hours that the study had to be discontinued. It seems possible that the mechanical process of vomiting was responsible for the sudden change from a negative to a positive balance. The fourth, represented by the lowermost curve, evidenced a clear-cut positive leucopenic response and this was accompanied by an allergic urticaria.

The charts for milk, wheat (toast), and egg are composite curves in that they represent the highest and lowest counts for each half-hour interval as manifested by all of the patients with food idiosyncrasy and by all of the controls. In each case the lower of the two composite areas represents those with idiosyncrasy. For milk there were six negative controls and three with idiosyncrasy, their resulting symptoms being asthma, colitis and eczema. The wheat graph represents four

negative controls and two with symptoms from this food, asthma and indigestion. The egg curves include four without symptoms and six

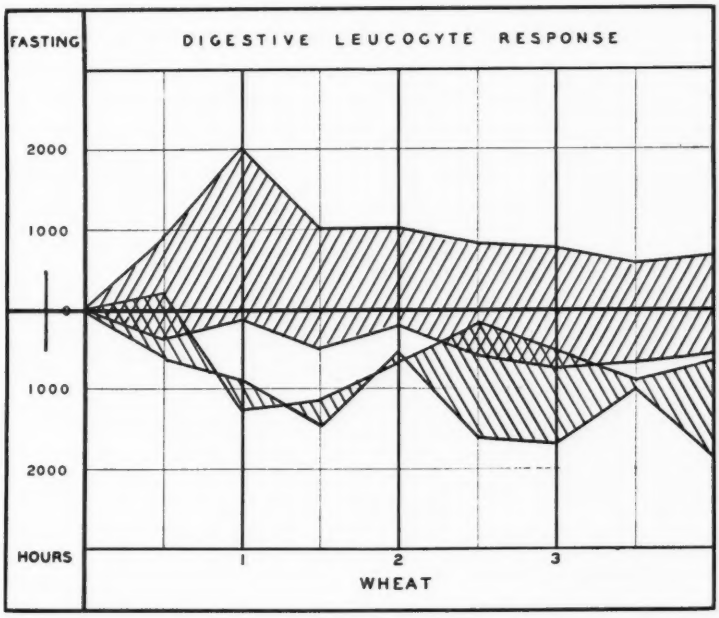

Chart 4.

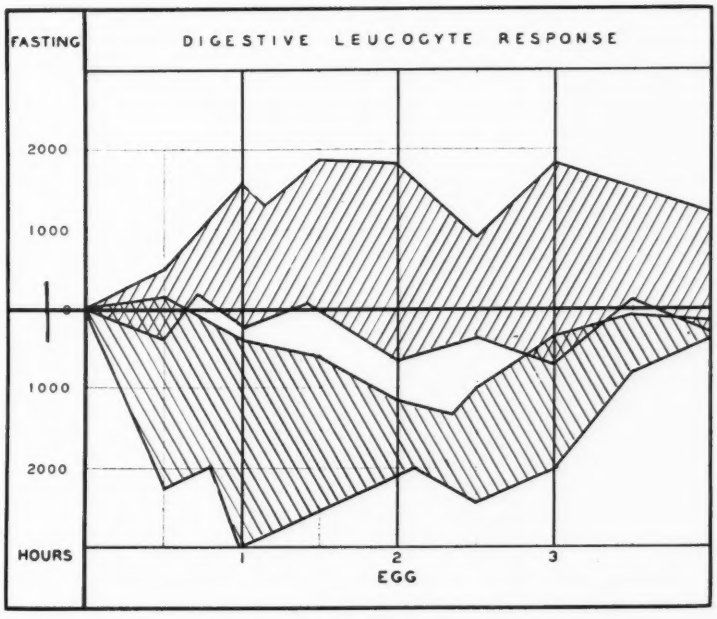

Chart 5.

with, including asthma, eczema, headache, and indigestion. The single vertical line in the fasting column represents the largest variation in

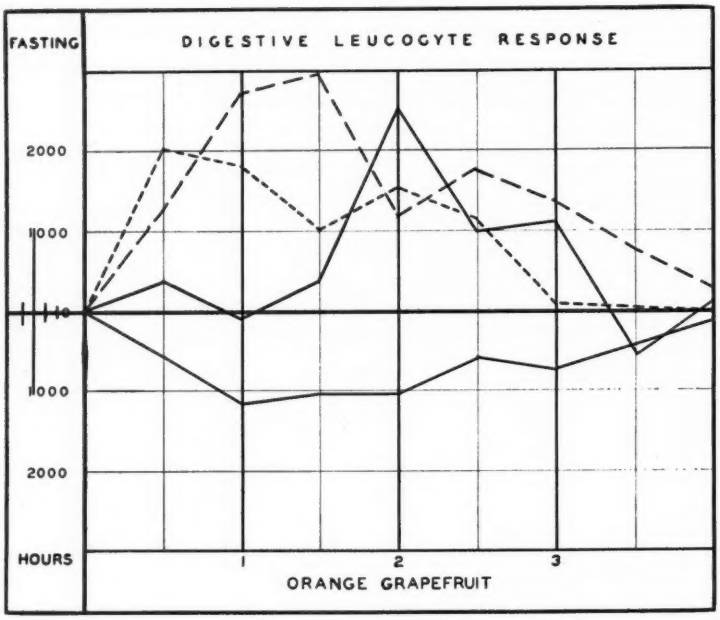

Chart 6.

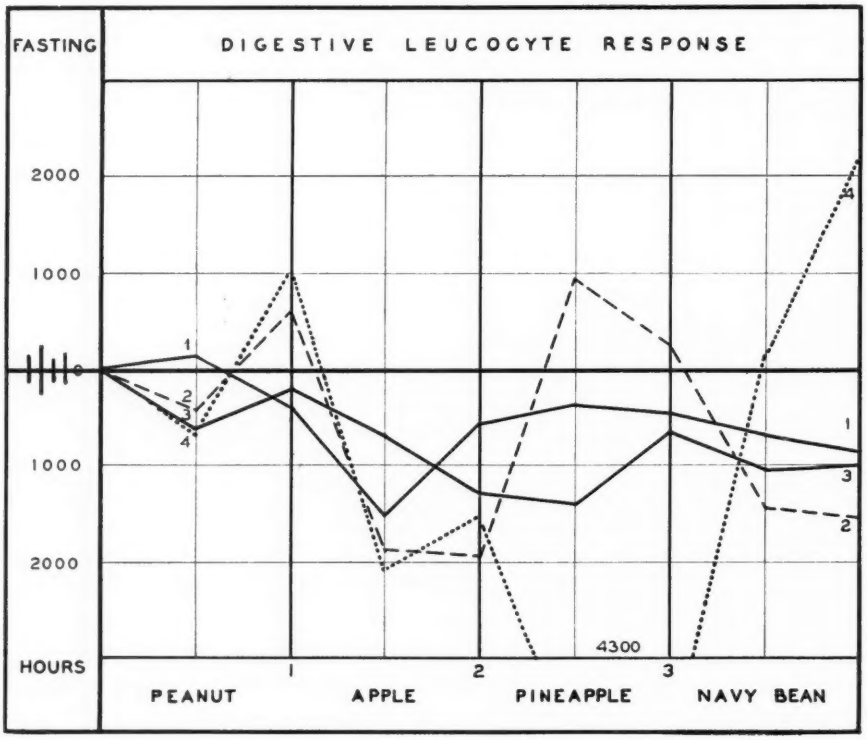

Chart 7.

the fasting counts of all of the curves represented. It becomes obvious from the milk, wheat, and egg charts that there is a definite tendency toward a lower range of the digestive leucocyte response in individuals with idiosyncrasy to these foods and that this is almost invariably represented by a definite leucopenia of varying degree.

The response to citrous fruits is of interest. The broken lines indicate negative controls. The lowermost line is a clear-cut leucopenic response in an individual in whom orange causes eczema. The next curve shows a leucocytosis on all counts except those at one hour and three and one-half hours, and yet the eating of orange resulted in nausea, vomiting and later a severe headache. This would appear to

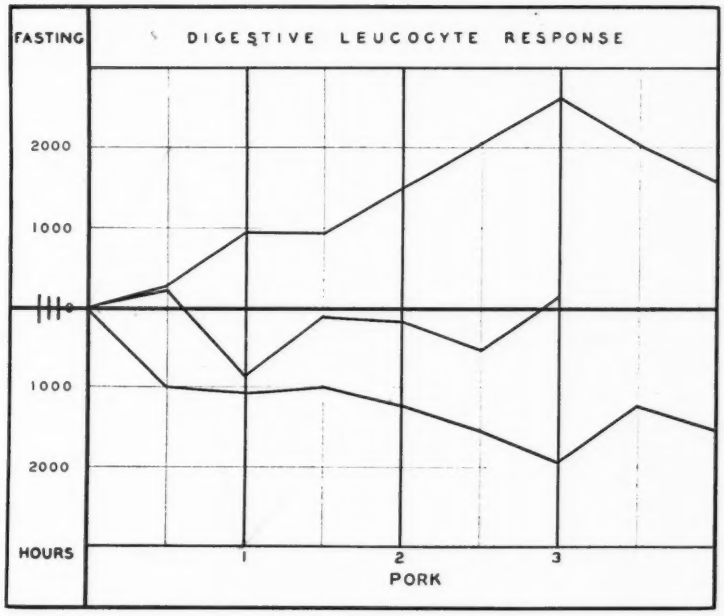

Chart 8.

be an exception to the rule as indicated in the preceding charts. However, the immediate high leucocyte increase in the two controls may indicate that the normal response to citrous fruits or foods containing organic acids of this type is that of a prompt leucocytosis. If this is so, the failure of the count to rise for the first ninety minutes may be of significance. This appears worthy of further study.

The miscellaneous chart representing curves for peanuts, etc., is rather incomplete, in that negative control tests were not made. All patients showed idiosyncrasies to the respective foods, and in each case there was a predominant drop in the white count. Peanuts caused dermatitis, apples produced migraine, pineapple, acute diarrhea, and navy beans promptly resulted in indigestion with nausea. The drop

in white count from navy bean, to 4,300 below the fasting level was the most pronounced that we have observed.

That there are exceptions to the apparent rule established by the preceding analyses is indicated in the charts for pork and potato. All three pork curves are from persons with definite idiosyncrasy thereto. In order, from above down, these persons experienced diarrhea with asthma and hives; acute acneiform dermatitis; and indigestion, following the eating of pork. It is of interest that the first person with pronounced leucocytosis showed a positive skin reaction to pork.

The highest of the curves for potato occurred in an individual who experiences asthma from potatoes, only after having eaten them several days in succession. She did not have asthma following the eating

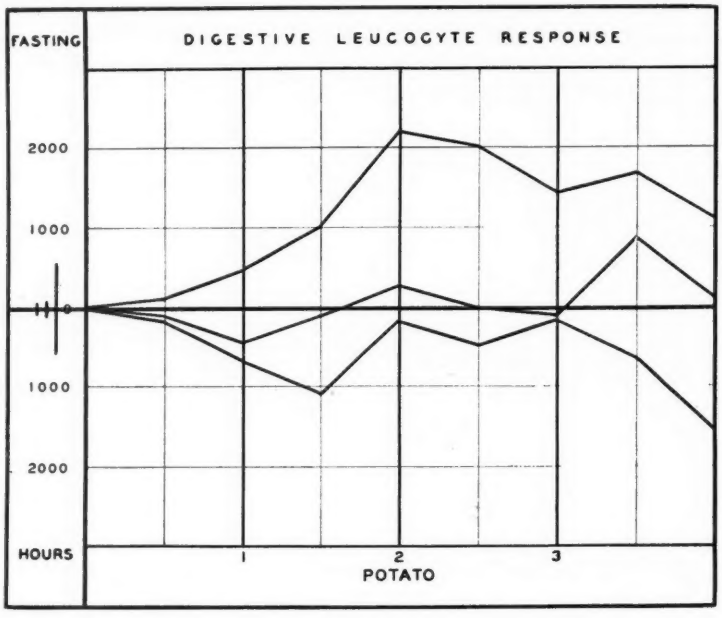

Chart 9.

of potatoes at the time of the test. The second curve likewise represents an individual very mildly sensitive who usually does not experience any symptoms therefrom, while the third experienced acute indigestion following the eating of the test potatoes.

The onion chart is of especial interest. The first two curves, which after a slight preliminary rise at the end of thirty minutes show a general low range, are for persons who experienced, respectively, asthma and indigestion following their ingestion. We desired a negative control for these two curves, for which purpose one of the technicians in the laboratory volunteered. She was very fond of onions and knew of no idiosyncrasy thereto, although in the past she had been subject to irregularly occurring headaches. Although she was used as a negative control, to our surprise she manifested a clear-cut

positive response. The following day she had a headache of migranous type, sufficiently severe to keep her in bed through the day. The factor of suggestion may be eliminated. Indeed it was not until a week later, when we were analyzing the records, that we realized the probable etiologic relationship. Skin tests were then made with onion extract, and she reacted positively.

In this series we have tested 26 persons with known idiosyncrasies. Of the 26 tests, 21 showed a leucopenic response. Foods included milk, wheat, egg, navy bean, pineapple, peanut, apple, tomato, pork, beef, orange, grapefruit, sweet potato, Irish potato, corn, onion, strawberry and chocolate. Foods failing at times to produce leucopenia were pork, Irish potato, chocolate, orange, corn.

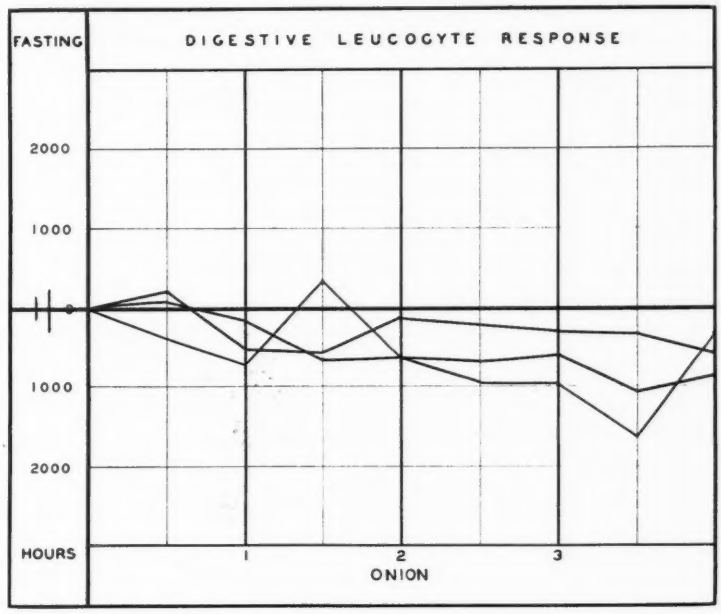

Chart 10.

Skin tests were done with these same foods. Among the 26 known offenders only 5 failed to react positively by leucopenic index while 17 failed to give positive skin reactions. This shows an 81 per cent correspondence between food allergy and leucocytic response as contrasted with 65.4 per cent correspondence with the results of skin testing.

Forty-three control tests were made with individuals not sensitive, so far as known, to the foods tested. In only 6 of the 43 were the reactions positive. One of the 6 was to tomato and the others were to staples such as wheat, egg, and milk. Tomato caused no symptoms but did produce a leucopenic response. Many months before, tomato had undoubtedly caused symptoms in this patient. The positive leucopenic response in this case may therefore be looked upon as an histori-

cal marker, evidencing past trouble. The same may be true with regard to the five positively reacting staple foods, although from the nature of the foods and the frequency with which they had been eaten, the persons tested were not in a position to know concerning them.

The suggestion might be made that the leucopenic response is a characteristic of the individual rather than of the individual's reaction to certain foods; that some persons react to all foods with a tendency toward leucopenia while others react with no leucocytic change or a leucocytosis. That this is not true is indicated by the results of multiple tests on the same individual. One person was tested with six different foods. Only one produced a leucopenic response. Three, who were tested with four different foods, showed only one positive reaction each, the remainder being negative. Three, tested with four different foods, showed two positives and two negatives each. Two, tested with three foods, showed two positive and one negative reaction. One, tested with three foods, showed one positive and two negative reactions. Three, tested with two foods, showed one positive and one negative reaction. One, tested with two foods, showed both positive.

Although we have not carried these studies out with mixtures of foods, it becomes obvious that food idiosyncrasy may color the digestive leucocyte response. When we realize that upward of 10 per cent of the population are frankly allergic, that an additional 50 per cent experience some minor allergic manifestation at one time or another, that food allergy is easily the most frequent form of sensitization, and that among the frankly allergic, staple foods such as milk, wheat, and egg are the most frequent offenders, we can readily understand that this is a factor which should be considered and ruled out in any study of digestive leucocytosis. Not only the type of diet selected but also the individual's reaction thereto may explain in part some of the divergent conclusions that have been reached in the past. We have found a definite practical application of those observations in facilitating the more accurate diagnosis of etiologic factors in food allergy.

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ORAL DESENSITIZATION TO COMMON FOODS*

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IN THE recent literature there is a definite increase in reports of symptoms due to food allergy but little on methods of overcoming this sensitization. Unnecessary or unusual foods may be avoided, but it is difficult to avoid entirely the more common ones. Hence, our object has been to desensitize patients to some of the common foods known to cause allergic symptoms.

As proved in the classical work of Schloss,[1] sensitization to food may be accomplished by hypodermic injection or by feeding the food to which the patient is sensitive. Schofield[2] and later Schloss desensitized children to common foods in three to eight months by administering gradually increasing amounts of the offending protein in capsules until tolerance was established. During the past five years we have tried a variety of methods of desensitization both oral and hypodermic. The oral method which follows has been the most satisfactory.

PROCEDURE

Definite sensitivity to a specific food was first determined; this was done by skin tests, elimination diets[3] and the reproducing of the patient's symptoms after eating the specific food to which he was sensitive. Oral desensitization was instituted if the patient was found to be sensitive to one of the common foods as: milk, wheat, egg, orange, tomato, or cocoa. With the exception of egg, the initial desensitizing dose contained about a milligram of protein. The whole egg, wheat, and milk were used, the powdered cocoa and the juice of tomato or orange. The protein content of the dilution was increased every four days so that at the end of a few months the patient was eating, without ill effects, a normal daily portion. If there was a recurrence of symptoms during the course of desensitization, the patient was instructed to drop back to the dilution given twelve or sixteen days previously. If the recurrence persisted, desensitization was delayed until the symptoms subsided. Occasionally the patient was desensitized to two foods simultaneously.

It has been much more difficult to desensitize patients with allergic symptoms to egg than to any of the other food proteins. At first the

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initial dose was one-tenth that required to give a positive skin reaction. Exacerbations occurred so frequently that the routine initial dose was reduced to 0.08 mg. of egg protein (one-fourth teaspoon of a solution containing one-fourth teaspoon of whole egg in two quarts of water).

Intolerance to milk has been rather common in patients with infantile eczema and in adults with gastrointestinal distress. In the latter there has usually been a history of a dislike for milk products and a history of eczema in infancy. The routine initial dose contained 0.8 mg. of milk protein, and the amount was usually increased so that at the end of three months an adult drank at least a cup of milk a day. In children this was gradually increased to three cups daily.

No particular difficulty was encountered in desensitizing patients to wheat, cocoa, orange, and tomato. The initial dose of each of the above contained about 1 mg. of protein.

The instructions as given to the patient follow. These contain the method of making the solution and a list of foods to be avoided. The necessity of not eating any food likely to contain the sensitizing protein was impressed on the patient and a list of such foods supplied.*

ORAL DESENSITIZATION TO EGG

Directions.—Beat an egg so that yolk and white are well mixed; then add the prescribed amount of egg to ordinary water and mix well. Take one teaspoon of the solution once a day unless otherwise directed. Throw away the rest of the solution. Make up a fresh solution every day. Use a dilution of the same strength every day for four days.

Mix ¼ teaspoon	egg with 2 quarts of water.	Take ¼ teaspoon.
Mix ¼ teaspoon	egg with 3 pints of water.	Take ¼ teaspoon.
Mix ¼ teaspoon	egg with 2 quarts of water.	Take ½ teaspoon.
Mix ¼ teaspoon	egg with 3 pints of water.	Take ½ teaspoon.
Mix ¼ teaspoon	egg with 2 quarts of water.	Take 1 teaspoon.
Mix ¼ teaspoon	egg with 3 pints of water.	
Mix ½ teaspoon	egg with 2 quarts of water.	
Mix ½ teaspoon	egg with 3 pints of water.	
Mix 1 teaspoon	egg with 2 quarts of water.	
Mix 1 teaspoon	egg with 3 pints of water.	
Mix 1 teaspoon	egg with 1 quart of water.	
Mix 2 teaspoons	egg with 3 pints of water.	
Mix 1 teaspoon	egg with 1 pint of water.	
Mix 2 teaspoons	egg with 1½ pints of water.	
Mix 1 teaspoon	egg with 1 cup of water.	
Mix 2 teaspoons	egg with 1½ cups of water.	
Mix 1 teaspoon	egg with ½ cup of water.	
Mix 2 teaspoons	egg with ¾ cup of water.	

*It is essential to give the patient a detailed list of foods to be avoided during desensitization, including all foods likely to contain the sensitizing protein. Such lists which are omitted here for lack of space will be included in the author's reprints.

Mix 1 teaspoon egg with ¼ cup of water.
Mix 1 teaspoon egg with 3 tablespoons of water.
Mix 1 teaspoon egg with 2 tablespoons of water.
Mix 2 teaspoons egg with 3 tablespoons of water.
Mix 1 teaspoon egg with 1 tablespoons of water.
Mix 4 teaspoons egg with 3 tablespoons of water.
Mix 2 teaspoons egg with 1 tablespoon of water.
Take 1 teaspoon of raw egg.
Take 1½ teaspoons of raw egg.
Take 2 teaspoons of cooked egg.
Take 3 teaspoons of cooked egg.
Take 4 teaspoons of cooked egg.
Take ½ cooked egg.
Take ¾ cooked egg.
Take a whole egg.
After this eat at least one egg every few days.

ORAL DESENSITIZATION TO MILK

Directions.—Take one teaspoon every day unless otherwise directed. Make up a fresh solution every day. Use a dilution of the same strength every day for four days.

Mix one teaspoon of milk with one quart of water.
Mix one tablespoon of milk with two quarts of water.
Mix one teaspoon of milk with one pint of water.
Mix one tablespoon of milk with one quart of water.
Mix one teaspoon of milk with one cup of water.
Mix one tablespoon of milk with one pint of water.
Mix one teaspoon of milk with ½ cup of water.
Mix one tablespoon of milk with one cup of water.
Mix one teaspoon of milk with ¼ cup of water.
Mix one tablespoon of milk with ½ cup of water.
Mix one teaspoon of milk with two tablespoons of water.
Mix one tablespoon of milk with ¼ cup of water.
Mix one teaspoon of milk with one tablespoon of water.
Mix one tablespoon of milk with two tablespoons of water.
Mix two teaspoons of milk with one tablespoon of water.
Take one teaspoon of milk.
Take 1½ teaspoons of milk.
Take two teaspoons of milk.
Take three teaspoons of milk.
Take four teaspoons of milk.
Take two tablespoons of milk.
Take three tablespoons of milk.
Take ¼ cup of milk.
Take ⅓ cup of milk.
Take ½ cup of milk.
Take ⅔ cup of milk.
Take one cup of milk.
For children: increase slowly until 3 cups of milk are taken daily.
For adults: increase to 2 cups of milk daily.

ORAL DESENSITIZATION TO WHEAT

Directions.—Use uncooked whole wheat flour. Add a small amount of water to the flour slowly so as to avoid lumps. Stir vigorously before eating. Use a dilution of the same strength once daily for four days. Make up a new solution every day. Take one teaspoon of the solution every day unless otherwise directed.

Mix ½ teaspoon flour with 1 quart of water.
Mix 1 teaspoon flour with 1½ quarts of water.
Mix 1 teaspoon flour with 1 quart of water.
Mix 1 teaspoon flour with 3 cups of water.
Mix 1 teaspoon flour with 1 pint of water.
Mix 1 teaspoon flour with 1½ cups of water.
Mix 1 teaspoon flour with 1 cup of water.
Mix 1 teaspoon flour with ¾ cup of water.
Mix 1 teaspoon flour with ½ cup of water.
Mix ½ teaspoon flour with 3 tablespoons of water.
Mix 1 teaspoon flour with ¼ cup of water.
Mix 1 teaspoon flour with 3 tablespoons of water.
Mix 1 teaspoon flour with 2 tablespoons of water.
Mix 2 teaspoons flour with 3 tablespoons of water.
Mix 1 teaspoon flour with 1 tablespoon of water.
Mix 2 teaspoons flour with 1½ tablespoons of water.
Mix 1 teaspoon flour with ½ tablespoon of water.
Mix 1 teaspoon flour with 1 teaspoon of water (Take all).
Eat ⅛ slice of bread daily for 2 days.
Eat ¼ slice of bread daily for 2 days.
Eat ½ slice of bread daily for 2 days.
Eat 1 slice of bread daily for 2 days.
Eat 1½ slices of bread daily for 2 days.
Eat 2 slices of bread daily for 2 days.
After this eat some wheat product daily.

ORAL DESENSITIZATION TO COCOA OR CHOCOLATE

Directions.—Mix ½ teaspoon of cocoa with 1 cup of sugar so that there are no lumps of either cocoa or sugar. Put into a container with cover and label this "Mixture No. 1." Mix ½ teaspoon of cocoa with ¾ cup of sugar. Put into a container and label this "Mixture No. 2." Each day add cold milk to the prescribed amount of mixture very slowly until a smooth paste is formed; then add enough milk to make it thin enough to drink. The amount of milk used does not matter. Be sure to drink all of it. Use the same mixture every day for four days.

Take ¼ teaspoon of mixture number 1
Take ¼ teaspoon of mixture number 2
Take ½ teaspoon of mixture number 1
Take ½ teaspoon of mixture number 2

Take 1 teaspoon of mixture number 1
Take 1 teaspoon of mixture number 2
Take 2 teaspoons of mixture number 1
Take 2 teaspoons of mixture number 2
Take 4 teaspoons of mixture number 1
Take 4 teaspoons of mixture number 2

Two new mixtures now must be made. They are to be labeled "Number 3" and "Number 4." Number 3: Mix 2 teaspoons of cocoa with ¼ cup sugar. Number 4: Mix 3 teaspoons of cocoa with ¼ cup sugar.

Take ½ teaspoon of mixture number 3
Take ½ teaspoon of mixture number 4
Take 1 teaspoon of mixture number 3
Take 1 teaspoon of mixture number 4
Take 2 teaspoons of mixture number 3
Take 2 teaspoons of mixture number 4
Take 4 teaspoons of mixture number 3
Take 1 teaspoon of cocoa mixed with 1 teaspoon of sugar.
Take 1½ teaspoons of cocoa mixed with 1½ teaspoons of sugar.
Take 2 teaspoons of cocoa mixed with 2 teaspoons of sugar.
Take 1 tablespoon of cocoa mixed with 1 tablespoon of sugar.
After this eat cocoa or chocolate at least every few days.

ORAL DESENSITIZATION TO ORANGE

Directions.—Squeeze an orange every day. Mix the juice with water as directed. Use once a day. Use a dilution of the same strength for four days. Take one teaspoon every day unless otherwise directed. Throw away the remainder of the mixture.

Mix 1 teaspoon of orange with ½ cup water.
Mix 1 tablespoon of orange with 1 cup water.
Mix 1 teaspoon of orange with ¼ cup water.
Mix 1 tablespoon of orange with ½ cup water.
Mix 1 teaspoon of orange with 2 tablespoons water.
Mix 1 tablespoon of orange with ¼ cup water.
Mix 1 teaspoon of orange with 1 tablespoon water.
Mix 1 tablespoon of orange with 2 tablespoons water.
Mix 1 teaspoon of orange with ½ tablespoon water.
Take 1 teaspoon of pure orange juice.
Take 1½ teaspoons of pure orange juice.
Take 2 teaspoons of pure orange juice.
Take 3 teaspoons of pure orange juice.
Take 4 teaspoons of pure orange juice.
Take 2 tablespoons of pure orange juice.
Take 3 tablespoons of pure orange juice.
Take ¼ cup of pure orange juice.
Take ½ cup of pure orange juice.
After this eat an orange or food containing orange at least every few days.

ORAL DESENSITIZATION TO TOMATO

Directions.—Use raw tomatoes. Squeeze out prescribed amount of pulp. Mix with water as directed. Use once a day. Make up a fresh solution every day. Use a dilution of the same strength for four days. Take one teaspoon every day unless otherwise directed. Throw away the remainder of the solution.

Mix 1 teaspoon of tomato with 1 cup of water.
Mix 1 tablespoon of tomato with 1 pint of water.
Mix 1 teaspoon of tomato with ½ cup of water.
Mix 1 tablespoon of tomato with 1 cup of water.
Mix 1 teaspoon of tomato with ¼ cup of water.
Mix 1 tablespoon of tomato with ½ cup of water.
Mix 1 teaspoon of tomato with 2 tablespoons of water.
Mix 1 tablespoon of tomato with ¼ cup of water.
Mix 1 teaspoon of tomato with 1 tablespoon of water.
Mix 1 tablespoon of tomato with 2 tablespoons of water.
Mix 1 teaspoon of tomato with ½ tablespoon of water.
Take 1 teaspoon of pure tomato juice.
Take 1½ teaspoons of pure tomato juice.
Take 2 teaspoons of pure tomato juice.
Take 3 teaspoons of pure tomato juice.
Take 4 teaspoons of pure tomato juice.
Take 2 tablespoons of pure tomato juice.
Eat ½ of a tomato. (This should be about 2½ inches in diameter.)
Eat ¾ of a tomato.
Eat 1 tomato.
After this either tomato or foods containing tomato should be eaten frequently.

RESULTS

The method as outlined above has been effective in desensitizing about fifty patients with allergic symptoms. For the most part these were small children with chronic allergic eczema. There were also a few adults with similar symptoms and a few patients with urticaria, acneiform and macular erythema of the face, and gastrointestinal symptoms due to intolerance to one of the above foods.

The method is suggested because it appears to be effective, inexpensive and can be accomplished at home using ordinary household measurements.

SUMMARY

A practical method of oral desensitization is suggested.

This method has been used in the treatment of skin eruptions and gastrointestinal symptoms due to sensitivity to specific foods.

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STUDIES OF SPECIFICITY IN MULTIPLE HYPERSENSITIVENESS BY QUANTITATIVE TITRATION AND ABSORPTION OF REAGINS*

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PRAUSNITZ and Küstner showed that constitutionally allergic individuals possess antibodies ("reagins") in their blood corresponding to the reacting allergens. These reagins were demonstrated by their method of passive transfer. The specific nature of such reagins has been confirmed by Coca and Grove[1] and Coca and Levine[2] who neutralized the skin sensitizing power of the reagins by previous mixing of the corresponding allergen and the serum under investigation, in vitro. Walzer and Bowman[3] employed this method for the purpose of studying the interrelationship between donkey, horse, and zebra epithelium. In 1932 Bosch, György and Witebsky,[4] in their studies of egg hypersensitiveness in eczematous children, were able to show that the dominating antigen of egg white was the albumen fraction itself. This was accomplished by exhausting the passively sensitized skin site with successive injections of various egg white fractions.

The employment of the foregoing methods in establishing the antigenicity of the test substance is obviously important. It becomes especially so when we have to interpret nonspecific reactions resulting from irritating factors in the material tested, hyperirritable skin, or the multiple reactions characteristic of the allergic state.

While the demonstration of sensitizing antibodies by means of the Prausnitz-Küstner technic is helpful in establishing the existence of a reaginic mechanism in the cases under investigation, it is of importance to determine not only qualitatively but also quantitatively, as far as our present methods permit, the concentration of each reagin in the patient's serum. As will be shown, this may provide a method for distinguishing more clearly major reagins corresponding to clinical symptoms in patients with multiple reagins. Although we fully realize that the quantitative preponderance of one or another antibody does not necessarily parallel *clinical* (tissue) *sensitivity,* nevertheless, the degree of antibody content in the serum may serve as an index of the *state of sensitization.*

In view of the fact that reagins seem to behave to a certain extent in a manner similar to other serum antibodies, the experience gained

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in regard to titration and absorption of antibodies in general was utilized in developing our procedure. Patients giving reaction to ragweed, timothy, tobacco, etc., were chosen for this investigation.

EXPERIMENTAL PROCEDURE

Antigens Used.—The ragweed and timothy extracts employed by us for routine tests in adults contained 0.01 mg. N per c.c., except where clinically pollen sensitive patients were tested, when extracts containing 0.001 mg. N per c.c. were employed. Our tobacco extracts varied between 0.06 mg. N per c.c. for Xanthis (turkish tobacco) and 0.09 mg. N per c.c. for Burley; Maryland contained 0.09 mg. N per c.c.; Virginia 0.07 mg. N per c.c. The usual quantity between 0.01 and 0.02 c.c. was used in intradermal testing.

The tobacco antigens were prepared in accordance with a modified Coca technic, the difference being in a rather prolonged dialysis against buffered saline (approximately three to four weeks) until the dialysate was clear of coloring matter. *Thin* cellophane bags were used. The extracts were standardized by the nitrogen method for the purposes of comparisons with the ragweed and timothy extracts used in our investigations. In this connection, we wish to emphasize that with possible exception of pollens neither the nitrogen nor the protein content is an absolute guide as to the degree of antigenicity of an extract. The latter must be determined clinically for each substance separately, until we have better means of determining antigenic values.

Method of Passive Transfer (Prausnitz-Küstner Reaction).—Perfectly normal individuals who gave no reactions to the antigens employed were selected as receptors. Into the upper and outer aspect of the arm, a number of sites were injected with 0.1 to 0.2 c.c. of the serum to be tested. Three days later these sites were tested with the antigen under investigation. Each experiment was carried out on at least three normal receptors.

PART I.

CASE HISTORY

Patient B was admitted to Mount Sinai Hospital in 1932, complaining of angina pectoris for the past four years. His past and family histories were negative for the more familiar allergic manifestations such as asthma or hay fever. Although he had never smoked, he had used snuff for thirty-five years. During the past fifteen years, he was supposed to have had a moderate hypertension 175/80 mm. Hg. His electrocardiograph, on admission, showed but slight evidence of myocardial damage. Skin tests with tobacco, ragweed, timothy, feathers, etc.,

resulted in a marked four-plus reaction to tobacco, slight (one-plus) to ragweed and negative reactions to foods and other inhalants.

In order to determine the presence of tobacco reagins (antibodies) in the serum of Patient B as well as to establish whether there was any quantitative relationship between the reagins for ragweed and tobacco, passive transfers were first made with whole serum. The result of these transfers indicated that he had marked reagins for tobacco and none for ragweed (Fig. 1).

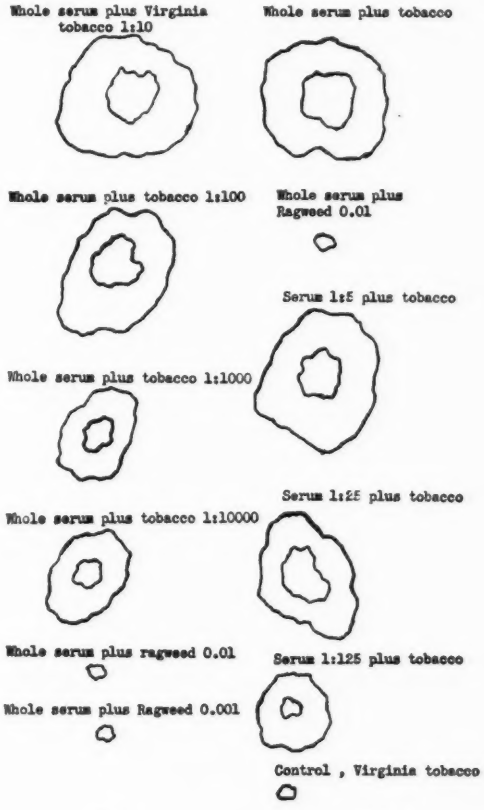

Whole serum plus Virginia tobacco 1:10
Whole serum plus tobacco
Whole serum plus tobacco 1:100
Whole serum plus Ragweed 0.01
Serum 1:5 plus tobacco
Whole serum plus tobacco 1:1000
Serum 1:25 plus tobacco
Whole serum plus tobacco 1:10000
Whole serum plus ragweed 0.01
Serum 1:125 plus tobacco
Whole serum plus Ragweed 0.001
Control , Virginia tobacco

Fig. 1. Fig. 2.

To establish the degree of sensitivity to tobacco antigen as well as the concentration of reagin, both were titrated quantitatively as shown in Table I.

The results indicate that Virginia tobacco diluted 1:10,000 still gives positive reactions when tested in a site passively sensitized with the whole serum (Fig. 1).

The second step was to determine the degree of reagin content in B's serum. This was done by progressively diluting this serum with buffered saline, 1:5, 1:25, and 1:125, injecting it into a normal skin

and testing it with undiluted Virginia tobacco 0.07 mg. N per c.c. according to the above described technic.

TABLE I

QUANTITATIVE TITRATION OF THE TOBACCO ANTIGEN BY MEANS OF PASSIVE TRANSFER OF UNDILUTED SERUM OF PATIENT B

	RESULT
Undiluted serum site tested with 0.01 c.c. of Virginia tobacco (0.07 mg. N per c.c.) (See Fig. 2.)	+++ to ++++
Site 1 undiluted serum tested with 0.01 c.c. of Virginia tobacco (0.07 mg. N 1:10) (See Fig. 1.)	+++
Site 2 undiluted serum tested with 0.01 c.c. of Virginia tobacco (0.07 mg. N 1:100) (See Fig. 1.)	+++
Site 3 undiluted serum tested with 0.01 c.c. of Virginia tobacco (0.07 mg. N 1:1,000) (See Fig. 1.)	+to++
Site 4 undiluted serum tested with 0.01 c.c. of Virginia tobacco (0.07 mg. N 1:10,000) (See Fig. 1.)	+to++

TABLE II

QUANTITATIVE TITRATION OF SERUM OF PATIENT B WITH VIRGINIA TOBACCO BY MEANS OF PASSIVE TRANSFER

DILUTION OF SERUM OF PATIENT B	VIRGINIA TOBACCO	RESULT
Site 1 1: 5	0.01 c.c.	+++
Site 2 1: 25	0.01 c.c.	+++
Site 3 1:125	0.01 c.c.	+

As is seen from Table II, positive reactions were obtained in each passively sensitized site even with serum dilutions of 1:125. Control sites tested with ragweed pollen extract were negative (Fig. 2).

In order to study the quantitative interrelationship between antigen and antibody in serum of Patient B, the following experiment was carried out:

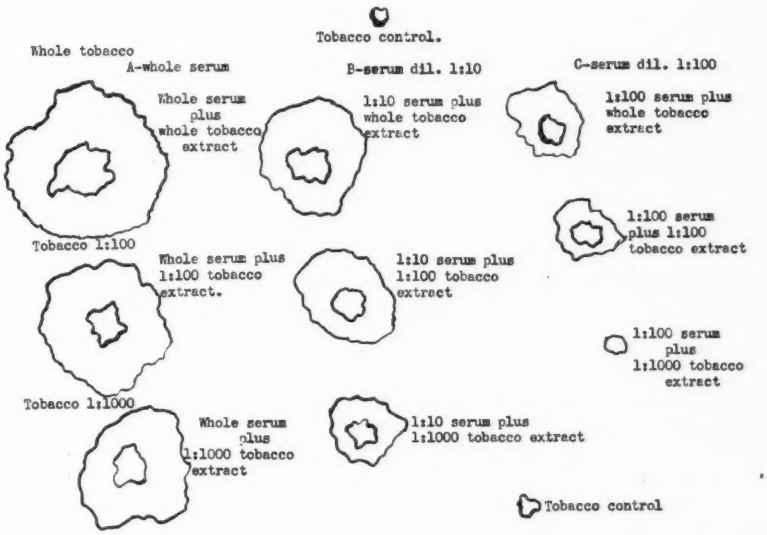
Several sites of three negatively reacting receptors were injected with 0.1 to 0.2 c.c. of Patient B, whole serum, serum diluted 1:10 and 1:100. Three days later each site was tested with undiluted tobacco extract, 1:100 and 1:1,000 (Table III).

TABLE III

QUANTITATIVE INTERRELATIONSHIP BETWEEN ANTIGEN AND REAGINS OF SERUM OF PATIENT B

	SERUM DILUTION	ALLERGEN DILUTION	RESULT
			Positive reaction
Site 1	Undiluted serum tested with	undiluted tobacco extract	+++ to ++++
Site 2	Undiluted serum tested with	1:100 tobacco extract	+++
Site 3	Undiluted serum tested with	1:1,000 tobacco extract	++
Site 4	Serum 1:10 tested with	undiluted tobacco extract	++ to +++
Site 5	Serum 1:10 tested with	1:100 tobacco extract	+ to ++
Site 6	Serum 1:10 tested with	1:1,000 tobacco extract	+
Site 7	Serum 1:100 tested with	undiluted tobacco extract	+
Site 8	Serum 1:100 tested with	1:100 tobacco extract	+
Site 9	Serum 1:100 tested with	1:1,000 tobacco extract	Negative reaction

As is seen from Table III, the upper limit of reagin content of serum Patient B was attained with a serum dilution 1:100 when tested with a dilution of tobacco extract of 1:100 (Fig. 3).


Tobacco control.
Whole tobacco
A-whole serum
B-serum dil. 1:10
C-serum dil. 1:100
Whole serum plus whole tobacco extract
1:10 serum plus whole tobacco extract
1:100 serum plus whole tobacco extract
Tobacco 1:100
1:100 serum plus 1:100 tobacco extract
Whole serum plus 1:100 tobacco extract.
1:10 serum plus 1:100 tobacco extract
1:100 serum plus 1:1000 tobacco extract
Tobacco 1:1000
Whole serum plus 1:1000 tobacco extract
1:10 serum plus 1:1000 tobacco extract
Tobacco control

"Brown" serum—Virginia tobacco extract—Straight transfers.

Fig. 3.

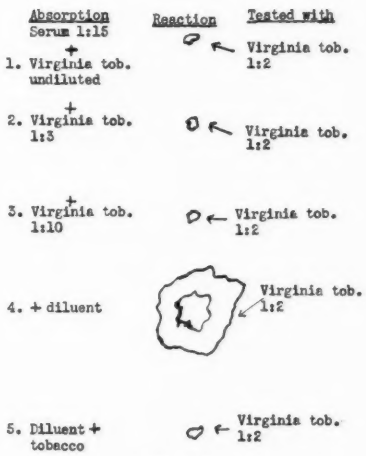


Fig. 4.

While such a degree of serum as well as antigen dilution in itself strongly suggests the specific nature of the above reaction, we also endeavored to absorb the tobacco antibody by means of tobacco antigen.

For this purpose the highest dilution of serum which gave a marked (three plus) reaction in the Prausnitz-Küstner transfer was used. Our previous findings indicated that a dilution of 1:15 was most suitable.

The experiment itself was carried out in the following way: Equal parts of serum diluted 1:15 were mixed with equal parts of, (a) extract of Virginia tobacco undiluted, (b) extract of Virginia tobacco diluted 1:3, (c) extract of Virginia tobacco diluted 1:10, (d) extract of Virginia tobacco diluent, and (e) diluent mixed with undiluted Virginia tobacco.

These mixtures were incubated for four hours at 37° C., and then placed in an ice box overnight. One-tenth to 0.2 c.c. of each of these mixtures were injected into the skin of normal receptors and tested, seventy-two hours later, with 0.01 c.c. of Virginia tobacco in a dilution of 1:2 (Fig. 4).

REACTION OF SERUM OF PATIENT B AFTER PREVIOUS INCUBATION WITH TOBACCO EXTRACT

TABLE IV

	SERUM INCUBATED WITH VIRGINIA TOBACCO	TESTED WITH	RESULT
Site 1	Serum 1:15 plus undiluted Virginia tob.	Virginia tob. 1:2	Negative
Site 2	Serum 1:15 plus Virginia tob. dil. 1:3	Virginia tob. 1:2	Negative
Site 3	Serum 1:15 plus Virginia tob. dil. 1:10	Virginia tob. 1:2	Negative
Site 4	Serum 1:15 plus diluent		Positive ++
Site 5	Diluent plus undiluted Virginia tob.		Negative

The above results prove that the previous addition of tobacco antigen to effective dilutions of serum containing tobacco reagin will fix the tobacco antibody and give negative Prausnitz-Küstner transfers. The upper limit of dilution of the tobacco antigen which is capable of inhibiting positive reactions was not yet reached in this experiment.

PART II.

The second phase of this investigation deals with the study of the identity of reagins in serums of patients who give multiple skin reactions and have multiple reagins (antibodies) corresponding to the positive skin reactions.

In view of the confusion resulting from the presence of numerous reagins the following questions usually arise: (1) Is there a single reagin (antibody) responsible for the numerous reactions? (2) Are there independent reagins (antibodies) for each corresponding antigen? (3) Are there some reagins (antibodies) which are independent, and others which stand for groups of antigens biologically or biochemically interrelated?

An answer to these questions was obtained in the study of the serum of Patient D, aged nineteen. This youth suffered from "family periodic paralysis," eczema and timothy hay fever. Because of the eczema he could not be tested directly for protein hypersensitiveness, and there-

fore had to be studied by the medium of passive transfer. Using this technic we found that Patient D had reagins to many foods and inhalants. Reagins for wheat, eggs, rye, rice, and corn were dominant. Clinically his hay fever coincided with timothy pollination. Several attacks of paralysis of the extremities followed smoking and the ingestion of large quantities of wheat in the form of bread and spaghetti.

In view of the fact that the largest reactions (four-plus) were obtained in the passively sensitized sites tested with timothy pollen,

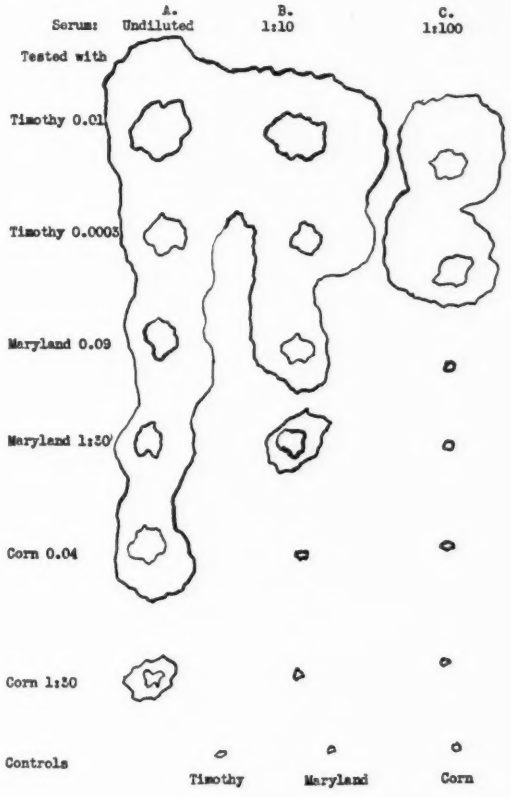


Fig. 5.

Maryland tobacco and corn, these were considered suitable for study from a quantitative point of view.

Serum of Patient D was injected into 18 different sites of three negatively reacting receptors as follows: Six sites were injected with 0.1 to 0.2 c.c. of undiluted serum, six sites were injected with 0.1 to 0.2 c.c. of serum 1:10, and six sites were injected with 0.1 to 0.2 c.c. of serum 1:100. Seventy-two hours later these sites were tested with (a) 0.01 c.c. of timothy (0.01 mg. N per c.c.), (b) 0.01 c.c. of timothy dilution 1:30, (c) 0.01 c.c. Maryland tobacco (0.09 mg. N per c.c.), (d)

0.01 c.c. of Maryland dilution 1:30, (e) 0.01 c.c. corn (0.04 mg. N per c.c.), and (f) 0.01 c.c. of corn dilution 1:30, as shown in Table V.

TABLE V (FIG. 5)

SITES CONTAINING SERUM OF PATIENT D

ALLERGEN TESTED		SERUM UNDILUTED REACTION	DILUTED 1:10 REACTION	DILUTED 1:100 REACTION
Timothy	0.01	++++	+++	++
Timothy	0.0003	+++	+	++
Maryland tobacco	0.09	+++	+	0
Maryland tobacco	1:30	++	+	0
Corn	0.04	++	0	0
Corn	1:30	+	0	0

As is seen from Table V, Serum D contains reagins in varying degrees against timothy, tobacco, and corn. It is evident, however, that timothy as well as Maryland tobacco extracts react in higher dilutions than corn.

In order to answer the question whether these antibodies are independent of each other, the following experiment was carried out:

Equal parts of serum and corresponding antigens were incubated at 37° C. for four hours and kept in the ice box overnight, as follows:

Sept. 25, 1934, a. 1 c.c. undiluted serum plus 1 c.c. timothy (0.01 mg. N per c.c.).

b. 1 c.c. undiluted serum plus 1 c.c. Maryland tobacco (0.09 mg. N per c.c.).

c. 1 c.c. undiluted serum plus 1 c.c. corn (0.04 mg. N per c.c.).

d. 1 c.c. undiluted serum plus 1 c.c. buffer saline.

Sept. 26, 1934, 0.1 c.c. of each mixture was injected into 12 skin sites of three negatively reacting subjects.

Sept. 28, 1934, each of these sites was tested as shown in Table VI.

TABLE VI (FIG. 6)

ROW	SITE 1	SITE 2	SITE 3
SERUM D INCUBATED WITH	TESTED WITH 0.01 C.C. OF TIMOTHY	TESTED WITH 0.01 C.C. OF MARYLAND TOBACCO	TESTED WITH 0.01 C.C. OF CORN
A. Timothy	Negative 0	Positive ++	Negative 0
B. Maryland tobacco (0.09)	Positive +++	Negative 0	Negative 0
C. Corn (0.04)	Positive +++	Positive ++ to +++	Negative 0
D. Buffer saline	Positive +++	Positive ++ to +++	Positive ++

It is clear from this experiment that in Row A, which consisted of sites sensitized with the serum treated with timothy extract in vitro, Site 1 gave a negative reaction when tested with its homologous antigen timothy. Site 2 reacted positively when tested with tobacco. This

indicates at once that after elimination of the timothy reagin, reagin for tobacco remains behind. The third site in this row, however, gave negative reactions when tested with corn antigen indicating that there was no corn antibody available, after preliminary incubation with timothy extract.

Row B, containing sites sensitized by serum incubated with Maryland tobacco in vitro, gave negative reactions on testing with its homologous tobacco antigen (Site 2), but yielded positive reactions when tested with timothy (Site 1). The third site in this row when tested with extract of corn was likewise negative, indicating no available corresponding corn reagin (antibodies).

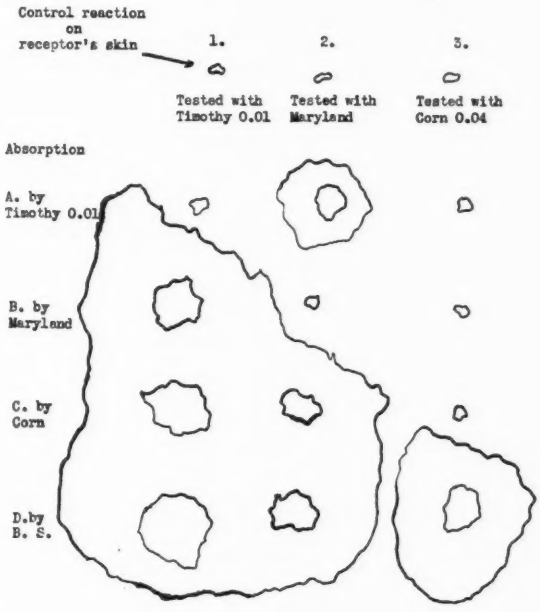


Fig. 6.

Row C, containing sites sensitized with a mixture of "D" serum and corn antigen, gave reactions in Sites 1 and 2 when tested with timothy and tobacco, indicating the presence of their corresponding antibodies, apparently not influenced by the previous incubation with corn. The third site, however, when tested with corn was completely negative, proving the specific nature of the reaction.

The negative reactions to corn in the sites sensitized by the timothy- and tobacco-fixed serums, respectively, on testing with corn antigen indicate an absence of a separate corn antibody. This would lead us to suspect that the corn antibody in this particular instance may not be a reaginic entity, but perhaps be related to the timothy or the tobacco antibody. From a serologic point of view it may be held that

the reagin to corn is a partial antibody sharing its existence with the independent timothy and tobacco reagins.

Corn nevertheless could play a rôle in inducing clinical hypersensitiveness. This last, as has been indicated by Coca, as well as by Teale,[5] is predetermined not only by the presence of reagins but also by the existence of "an atopic state of the shock organs" whose vulnerability results in the development of symptoms. Information as to the shock organ can only be deduced from the patient's history and clinical manifestations. From a practical point of view treatment with timothy pollen extract may suffice to protect this patient against corn so that the latter need not be taken into consideration in desensitization.

The rôle of tobacco reagins in ragweed hay fever cases and thromboangiitis obliterans patients is in the process of investigation.

DISCUSSION AND SUMMARY

A review of these investigations indicates that in patients with multiple hypersensitiveness demonstration of corresponding reagins by the Prausnitz-Küstner technic gives us only qualitative information as to the nature of the antibodies present.

This method affords no insight in respect to the concentration of reagins in the serum, their independence or mutual interdependence (complete or partial), which may exist as a result of stimulation by biochemically related antigens.

A true evaluation of such factors can only be obtained by both quantitative titration and absorption of the respective reagins. This method carried out in the study of the serums of our cases, one of whom reacted to tobacco and ragweed, and the other who with the ordinary passive transfer was shown to have antibodies for various cereals, meats, fish, and vegetables, yielded the following information:

1. Quantitative titration of the tobacco reagins in Case 1, who had coronary artery disease with angina pectoris associated with clinical tobacco hypersensitiveness, disclosed that the upper limit of reaction was reached with a serum dilution of 1:100 and tobacco antigen (Virginia 0.07 mg. N per c.c.) in a dilution of 1:100. This would indicate a high degree of sensitivity to the tobacco extract employed.

2. Previous addition of tobacco extract to the serum of this patient in vitro, inhibited sensitization of normal skin on passive transfer, indicating absorption of the related antibody.

In Patient 2 with the diagnosis of family periodic paralysis and eczema, who displayed multiple sensitivity and had multiple reagins to timothy, corn, tobacco, etc., corresponding to his clinical symptoms, a study of these reagins yielded the following data:

1. Quantitative titration of reagins for timothy, tobacco, and corn indicated that these were present in various concentrations.

2. Preliminary addition of timothy extract to serum in vitro exhausted the reagin for timothy and corn but not for tobacco.

3. Previous addition of tobacco extract to the serum fixed the reagin for tobacco and corn but not for timothy.

4. Addition of corn extract to this serum absorbed the corn antibody but did not influence the tobacco or the timothy antibody.

It may therefore be concluded that in the patients studied the major reagins were those for tobacco and timothy. These were specific and independent. Consequently the skin reactions were due to a reaginic mechanism.

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PRACTICAL PROCEDURES IN THE INVESTIGATION OF CERTAIN ALLERGIC DERMATOSES*

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THE following outline does not pretend to be complete. It is intended to serve only as a rough guide, as a framework upon which to build the more detailed investigative procedures necessary in each specific case. This schematic presentation has as its basis neither theories nor unalterable facts, but presents merely the actual routine followed during the last five years, both at our clinics and in office practice. We hope that the publication of this procedure may be of some value to those who are engaged in the study and treatment of allergic dermatoses.

Many important allergic—and some presumably allergic—dermatoses have been but briefly mentioned or deliberately omitted; several of these, because studies have not, as yet, led to procedures of more than limited practical diagnostic and therapeutic usefulness (tuberculids, trichophytids, epidermophytids, moniliids, syphilids, etc.); others, because the nature of the presumptive allergen is, as yet, unknown, and routine testing is therefore impossible (infectious eczematoid dermatitis, multiform and nodose erythemas, dermatitis herpetiformis, rheumatic eruptions, purpuras, etc.). While investigative and particularly research work naturally includes skin tests in these dermatoses, their detailed discussion would have extended this summary without, in our opinion, adding materially to its practical value.

INTRODUCTORY GENERAL DATA

(Regardless of the type of dermatosis)

1. Name, age, sex, nationality, race, previous illness, personal and family history, etc.

2. Occupation.

3. Hobbies and avocations (sports, games; pets of all kinds, the substances used in their care, and the parasites to which they are subject; photography, etc.).

4. Medicaments (topical and internal).

5. Seasonal incidence, cyclic course, etc.

6. Dietary habits (excesses [iodized salt, etc.]), (deficiencies [vitamins, etc.]).

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7. Skin qualities and general appearance—dry and fissured; or oily skin; hyperidrosis, etc.

8. Endocrine, vasomotor, and nervous disturbances.

I. INVESTIGATIONS FOR THE DIFFERENTIAL DIAGNOSIS OF TRUE ECZEMA (CONTACT DERMATITIS, DERMATITIS VENENATA TYPE) AND ECZEMATOID DERMATOSES (ATOPIC DERMATITIS, I.E., DISSEMINATE NEURODERMITE; AND SEBORRHEIC DERMATITIS)[8-15]

A. Clinical appearance of eruption as an aid in differential diagnosis.

1. Distribution and localization of eruption (localized or disseminate, sharply demarcated or not, symmetrical or not; sites of predilection—for example, primarily in exposed areas or not, on seborrheic areas or not, intertriginous or not, on extensor or flexor surfaces, on face, or on feet and on hands).

2. Characteristic or primary efflorescence (polymorphous or not, weeping, lichenification, pigmentation, scaling; papular, vesicular or not [vesicles in eczematous appearing eruptions are almost pathognomonic of true eczema, i.e., contact type dermatitis]).

B. History as an aid in the differential diagnosis.

1. Family and personal history of atopic conditions (hay fever, asthma [not cardiac asthma], infantile eczema); when positive in a case of eczematoid dermatitis, this history speaks in favor of an atopic dermatitis, i.e., disseminate neurodermite.[8]

2. Family and personal history of seborrheic conditions ("kerose" of Darier, oily skin, seborrheic pityriasis, alopecia, acne, seborrheic dermatitis); these when present in excessive degree speak somewhat in favor of seborrheic "eczematoid" dermatitis.

3. Personal history of eczematous mycoses (dermatophytids) or previous truly eczematous eruptions, i.e., contact type (when present speaks in favor of contact dermatitis).[14, 15]

4. History of occupational, home, and social contacts.

(a) Chemical: dyes, metals, caustics, bleaches, detergents, plants, insecticides, lacquers, paints, varnishes, cosmetics, topical remedies (prescribed and proprietary), internal medication, etc.

(b) Physical: heat, cold, actinic effects, moisture, friction, and other traumas.

(c) Combinations of physical and chemical agents.

5. History of seasonal or periodic occurrence.

Atopic dermatoses often exacerbate seasonally with (in New York) a peak in the autumn and early winter.* Seasonal or periodic recurrences may give a clue as to the etiology in certain contact dermatitides, such as plant dermatitis; or in certain cases of vocational or avocational dermatoses. The chronology of recurrences is, for example, of first im-

*We have found that most of our patients with seasonal attacks of atopic dermatitis are skin hypersensitive to, and have reagins to the seasonal pollens, even in the absence of hay fever or asthma.

portance in certain occupational eczemas which improve while the patient is away from certain kinds of work and exacerbate when this work is resumed.

6. Topical remedies previously used (more or less recently).

While this investigation does not help to ascertain the etiology or nature of the original complaint, it is true, nevertheless, that practically all topical remedies, proprietary or *prescribed,* can sensitize and cause eczematous dermatitis; and in our experience a relatively high percentage of cases of contact dermatitis is due to some remedy applied to the original lesion, which may have been insignificant and often of a different nature from the contact dermatosis which brings the patient to the physician (mercury applied to seborrheic dermatitis or impetigo, local anesthetics applied to itching areas, sulphur to scabies, germicides used in treating cuts, wounds, or as general disinfectants in surgery, etc.). One of us has called attention to the fact that contact dermatitis from local anesthetics may run a very protracted course, the dermatosis and particularly the itching very often persisting many weeks after the last contact with the offending anesthetic.[14, 21, 22] This investigation of the remedies used often brings to light a combination of atopic and contact dermatitis, or more frequently of seborrheic and contact dermatitis.[13, 14]

C. Clinical and laboratory investigations to establish differential diagnosis.

If after the above considerations the differential diagnosis of contact dermatitis, atopic dermatitis, and seborrheic dermatitis is still uncertain or impossible, the following investigative measures are employed:

1. Patch tests with 20 or more standard eczematogenous substances; numerous positives speak in favor of a contact dermatitis.[8, 13, 14]

We employ the following as standard substances for routine patch-testing:

1. Copper sulphate, 1 per cent aqueous solution.
2. Sodium arsenate, 10 per cent aqueous solution.
3. Potassium dichromate, ½ per cent aqueous solution.
4. Mercury bichloride, 1:1,000 aqueous solution.
5. Nickel sulphate, 5 per cent aqueous solution.
6. Novocaine, 1 per cent aqueous solution.
7. Metaphen, standard solution.
8. Mercurochrome, standard solution.
9. Nicotine salicylate, 10 per cent aqueous solution.
10. Tincture of pyrethrum, 20 per cent tincture.
11. Butesin picrate, 1 per cent in white vaseline.
12. Resorcin, 1 per cent aqueous solution.
13. Quinine hydrochloride, 1 per cent aqueous solution.
14. Paraphenylendiamine, 2 per cent in white vaseline.
15. Orris root, powdered.

16. Potassium iodide, 25 per cent in petrolatum.
17. Formalin, 5 per cent aqueous solution.
18. Iodoform, powder.
19. Trichophytin, 1:10 (Lederle).
20. Oidiomycin, 1:10 (Lederle).
21. Old tuberculin, 1:10.
22. Para red (deep), powder.
23. Para red (light), powder.
24. Sudan III, 5 per cent in mineral oil.
25. Methyl orange, 5 per cent aqueous solution.
26. Rhus toxicodendron (Lederle), extract diluted 1:5,000 in acetone.
27. Ordinary adhesive plaster.

2. Scratch tests or intracutaneous tests with a series of common atopens. (If there are numerous wheal reactions, this speaks in favor of atopic dermatitis.)

3. Blood counts for eosinophilia. (If eosinophiles are markedly increased, it speaks somewhat in favor of atopic dermatitis; if they are not increased, this does not rule out this condition.)

If all the above investigative procedures lead to negative results, seborrheic dermatitis must be more seriously considered as a possible diagnosis. If number (1) is positive and numbers (2) and (3) are negative, the combined evidence would favor the diagnosis of contact dermatitis. If, vice versa, number (1) is negative and numbers (2) and (3) are positive, this speaks for atopic dermatitis. While if numbers (1), (2), and (3) are positive, the result suggests a possible combination of contact eczema and atopic dermatitis.

(The diagnostic measures discussed apply to some extent to the differential diagnosis between infantile eczemas of the atopic, seborrheic, and contact types.)

II. INVESTIGATION OF TRUE ECZEMA, I.E., A PROVED CASE OF CONTACT DERMATITIS (DERMATITIS VENENATA) IN ORDER TO DETERMINE THE SPECIFIC ETIOLOGY[1-6, 10-15]

A. The localization of the first appearance, or the site of predilection of the eruption directs attention to certain substances.

In general the face and scalp are first affected from hair dyes, cosmetics, etc.; neck and face are first affected from furs, fur dyes, collars, scarves, necklaces, etc.; hands and forearms are first affected from occupational substances, gloves, soaps, cleansers, etc.; the torso is first affected from rayon, silk, wool, clothing in general, rubber girdles, substances used in massaging, bath salts, etc.; feet and legs are first affected from shoe leather, shoe polishes, sock finishers, sock dyes, etc.; ring fingers, wrist, garter buckle areas, and lobes of the ears are first affected from metal, bakelite, celluloid, etc.; spectacle areas from metal or artificial tortoise shell; and so on, for a list infinitely long.

B. The occupation of the patient directs attention to certain substances.

For this investigation, it is necessary to know or to become acquainted with the multitudinous eczematogenous substances which represent the different hazards in different occupations. It would be impossible to submit here a list of the various trades and professions and of the eczema-producing substances peculiar to each. Reference must be made to text-books.[1, 2, 3] Common industrial causes of contact eczema are the following: dyes, bleaches, soaps, detergents, lacquers, paints and finishes, turpentine, plants, woods, glue, rubber and vulcanizers, cement, flour, spices, yeasts, metals and metal polishes, quinine, formalin, and other chemicals, celluloid and bakelite, and all the innumerable substances connected with the manufacture and finishing of synthetic and natural products.

C. The patient's hobbies direct attention to certain substances.

Here again, space permits the mention of only a few examples: in the case of horsemen—leather and leather polishes, materials used in cleansing and disinfecting stables, etc.; in the golfer—plants and grasses, the leather and wood of golf clubs, the golf gloves, club polishes, taped handles, etc.; in the hunter—plants and grasses, gun oil and gun polishes, etc.; in the amateur photographer—the chemicals used; in the mah jong player—lacquered tile; in the violinist—rosin, chin rest, wood, or wood finish. In the case of patients having pet animals, not only the animals' hair but also the substances employed in their care and cleanliness are to be considered.

D. The investigation of practically ubiquitous causes.

Once again, the list is incalculably long. In practically all women, the ingredients of cosmetics, such as orris root, perfumes, soaps, mascara, coloring materials, hair and lash dyes, face creams, massage creams, wave-set and other lotions, are suspect; and in practically all men, shaving materials, soaps, hair lotions, brilliantine, etc.; and in all children, all toys. In persons of all ages, shoes, socks or stockings, their dyes and finishes, hatbands, wrist watch straps, garters, nickel (coins, etc.) must be considered. In practically all homes, soaps, insecticides, disinfectants, floor and furniture polishes, anti-moth preparations, plants, phenol and formalin derivatives, bakelite, rubber and its accelerators, etc., are suspect. Contact with printer's ink and rotogravure colors is almost universal. (It is here necessary to consider not only the substances used by the patient but also those used by others in the patient's environment—see *F* in this group.)

E. Furthermore, as specifically mentioned under I, B, 6, all remedies used in previous treatment are suspect and must be applied as patch tests. Moreover, although rarely, certain eruptions of true eczematous (contact type) dermatitis can be caused by ingestion and the hematog-

enous distribution of the causative agent. The best examples of this are the eczematous eruptions due to quinine, to urotropin (formaldehyde), etc.[14, 21]

F. Substances used by persons in the patient's environment.

In the search for possible causative agents, the dyes, topical remedies, cosmetics, etc., used by others in the patient's environment must be considered. We have seen, for example, a case of contact dermatitis in a husband caused by an antipruritic lotion used by the wife, and two instances in which a mother had contact dermatitis from washing the clothes of a child who had been using a proprietary antipruritic ointment.

G. Fungi of various genera can cause epidermal hypersensitivity and eruptions of contact-dermatitis-type (eczematous and dyshidrotic "ids"). It is quite possible that other microorganisms can cause similar dermatoses. (Br. Bloch's "microbids," and "bacterids" of Darier.) Unfortunately, a detailed discussion of these eruptions would prove too lengthy for this brief outline. Such etiologies, however, must be considered either as the direct cause of the dermatitis under investigation, or as contributory factors by causing an original eczematous sensitization to fungous products with ensuing polyvalence to include contact substances, or as complicating factors of a contact dermatitis originally caused by nonliving agents.[4, 14, 16, 17, 18] Sensitizations of the epidermis to the products of microorganisms, i.e., eczematous "ids," are here not differentiated from contact dermatitis; from an immunologic standpoint, the pathogenesis seems analogous if not identical.[16, 18]

(The statements under heading II apply in a great measure to infantile eczema of the contact dermatitis type.)

III. THE SPECIFIC INVESTIGATION OF A PROVED ATOPIC DERMATITIS (NEURODERMATITIS DISSEMINATUS)

The specific etiologic agent or agents of a particular case are often impossible to ascertain. Scratch or intradermal tests—the demonstration of atopic reagins—diets and environmental control are the only known methods whereby the presumptive etiology may be ascertained. Skin tests are of very limited usefulness for, as a rule, one gets many strongly positive reactions and often finds reagins to many of these substances. Some investigators even doubt whether *any* of the substances which elicit the so-frequent positive wheal reactions and to which reagins can so frequently be found are the actual causative agents of this dermatosis. The polysensitivity of many of these cases makes it impossible to eliminate all the possible causative factors. This statement is particularly true when one considers that not only foods but also *inhalants*[9] and other environmental atopens of an ubiquitous and sometimes indispensable nature may be among the possible offending substances. Elimination diets plus allergen-free rooms would seem to be

the logical mode of approach to decide the significance of the positive skin tests and to carry out investigation and therapy by elimination. Such an investigation might show that, although many positives with specific reagins were encountered in a given case, only one or a few played the actual causal rôles. Since this method of investigation is, in most instances, not feasible at present, the results of the skin tests could not be checked clinically and have been of but little benefit to the average case; accordingly, we believe it inadvisable to subject the patient to this method of approach unless all other therapeutic measures have failed.

This does not mean that those patients in whom there is a doubt as to the diagnosis between neurodermite, contact dermatitis, and seborrheic eczema should not be tested at once with a routine series of atopens, as already outlined under I, C.[8, 10, 11]

What has been said about neurodermatitis disseminatus in adults applies *mutatis mutandis* to the atopic form of infantile eczema.

IV. THE SPECIFIC INVESTIGATION OF URTICARIA[4, 7, 28]

From the theoretic point of view, scratch or intradermal tests would appear to promise the greatest success in urticaria. Paradoxical as it seems, however, it is precisely in urticaria that we have found all forms of skin tests to be of very little value. In cases in which the skin tests with the actual etiologic agent have produced a positive wheal reaction, the patient has, as a rule, previously known of his or her specific intolerance. On the other hand, most urticarias of unknown etiology may be divided into three groups, as far as skin testing is concerned: first, those with such marked dermographism that direct testing is impossible; second, those in which skin tests produce no positive reactions; and third, those in which there are positive wheal reactions to numerous foods and inhalants. In this third class the practical value of the skin tests is reduced to almost zero by the factors enumerated in the discussion of skin tests in atopic dermatitis (see III).

It is to be hoped that here, too, allergen-free rooms plus simultaneous elimination diets may lead to a more precise knowledge of the significance of positive tests. We are impressed by another paradox concerning urticaria: namely, though the urticarial wheal is the characteristic skin test response in atopy, the majority of urticarias in our material does not seem to be of atopic nature (not familially associated with asthma, hay fever, and atopic dermatitis—and no reagins).[28]

Our routine practical investigation of urticaria follows.

A. Elimination of drugs.

The patient is questioned concerning the ingestion of drugs, as specified under V, below. In our material, the drugs found most frequently to blame in urticaria are: (1) aspirin and other salicylates; (2) iodides

and bromides (iodized salt! bromo seltzer! bromoquinine laxative!); (3) barbiturates; (4) morphine derivatives (codeine, etc.); (5) plant derivatives (balsams, resins, etc.); (6) phenolphthalein; (7) ipecac; (8) antipyretics and analgesics (pyramidon, quinine, etc.); (9) arsphenamines.

This list could be indefinitely extended to include the drugs less frequently producing urticarial eruptions.[5, 6, 7, 20]

B. Elimination of foci of infection.

Here the dentist, otolaryngologist, gastroenterologist, and internist must be called upon. While the gallbladder, the teeth, and the tonsils are in our material, the most frequent causative foci, others also play a rôle.

C. General management.

Purging with calomel and other laxatives, ingestion of mineral oil before and during each meal, the administration of adsorbent substances after meals (kaolin, charcoal, etc.) may relieve many urticarias which seem to be of gastrointestinal origin.[27] These measures, together with drugs affecting the vegetative nervous system (atropin, pilocarpin, adrenalin, ephedrine and gynergen [ergotamine tartrate]), plus autohemotherapy and calcium, belong to our standard treatment. Every patient with urticaria of long standing deserves, however, a most thorough and exhaustive medical check-up. Such diverse conditions as neoplasms, blood dyscrasias, neurologic diseases, metabolic diseases, intestinal parasites, bird and animal itch mites, brucella abortus infection, and endocrine disturbances including thyrotoxicosis may be mentioned as among the possible and not too infrequent causes. It may be mentioned that not only foods, drugs, and foci of infection, but also inhaled substances such as orris root and dust, and external contact substances such as wool, silk, dyes, etc., can cause urticaria.

That which has been said about urticaria is, in a great measure, applicable to angioneurotic edema of Quincke, except that in our material we have had no true case of Quincke's edema with positive wheal reactions to skin tests carried out with the usual methods.

V. INVESTIGATION OF DERMATITIS MEDICAMENTOSA[4-6, 19-22]

Drugs are among the most important allergens to be considered in allergic manifestations in general, and in allergic dermatoses in particular. The use of drugs is today an almost universal habit, and apparently the manifestations of drug idiosyncrasy can vary from blood dyscrasias to angina pectoris, from acute yellow atrophy to manic and psychotic states, from nodose erythemas to fixed drug eruptions, from eczematous, urticarial, multiform erythema-like, morbilliform, roseola-like, and scarlatiniform exanthems to acneform eruptions and furunculosis, from pityriasis rosea-like eruptions to pictures resembling sarcoma or granuloma fungoides, blastomycoses, gummas, or tuberculids, lichen planus, or herpes simplex and zoster. We therefore devote a large portion of

the time spent questioning the patient with an undiagnosed dermatosis in endeavoring to ascertain each and every drug taken within a reasonable length of time antedating the eruption. Patience and skill here often bring astonishing discoveries and not infrequently unexpectedly satisfactory results. It is useless, however, to ask: "What drugs do you take?" or, "Are you taking any medicine?" Our method is rather the following: "Do you suffer from headaches? What do you take for them? Have you ever taken aspirin, pyramidon, etc.? How long ago did you last take it? Do you sleep well? What do you take for sleeping? How are your bowels? When irregular, what do you do for them, ex-lax, agarol, etc.? Do you feel well or run down? Do you take tonics, blood purifiers, or herb teas? Have you pain at menses? Do you take pills or patent medicines for them? Have you hangovers, and what do you do for them? Do you have stomach upsets, and what do you use against them? When have you been to the doctor, the dentist, last and for what? What did he prescribe? Have you had any injections? How are your sinuses, and what do you use for them (intranasally, etc.)? Is the package of salt in your kitchen marked iodized?"

It is well to recall that not only drugs actually ingested, but also those injected or administered in suppositories such as quinine, resorcin, analgesics, etc., or employed as enemas or douches; or even simply used in tooth pastes and mouth washes, such as ipecac, phenolphthalein, etc.; or in some cases those only applied to cuts, abrasions, wounds, pyodermas, etc., or even to the uninjured skin, can cause dermatitis medicamentosa in sufficiently susceptible individuals.[14, 21, 22]

We believe that the above gives an idea of the mode of specific questioning, the manner of focusing the patient's attention, and the amount of detailed inquiry which we have found necessary—and profitable! The questioning must include inquiry as to specific ailments, and then the actual names of remedies which may have been employed.

Of course, the type of eruption often indicates the drug which is most suspect. On the other hand, present skin test methods are generally useless unless the eruption is frankly eczematous or erythrodermic (rare exceptions are found in some cases of urticarial drug eruptions from arsphenamine, quinine, ipecac, etc., with scratch tests; and in some acneform or fungating bromodermas and iododermas with patch tests).

In the erythrodermic and eczematous drug eruptions from arsphenamine, quinine, chloral hydrate, ipecac, ephedrine, codeine, etc., the patch test is valuable provided it be applied at the right time, by avoidance of testing during the refractory period (frequently nine to eleven weeks long), which often immediately follows the dermatosis; and provided it be applied, read, and evaluated correctly.

Since skin tests are of no aid in most cases of dermatitis medicamentosa, the etiology can, as a rule, be proved only by clinical test of elimination and renewed usage.

In many cases, elimination alone must suffice, as the effect of renewed usage might prove disagreeable or dangerous. It is to be emphasized that many drug eruptions can persist weeks, months, or even years after the last use of the offending drug. For example, urticaria from barbiturates or aspirin, etc., can persist for months after cessation of usage. Arsphenamine dermatitis sometimes apparently begins even weeks after the last injection, and bromodermas and iododermas may continue in a florid and progressive state years after the last employment of these drugs. This persistence must be remembered in the evaluation of the results of the elimination.[19-22]

VI. MISCELLANEOUS SKIN TESTS[4, 7]

We shall be brief here. The diseases we include are a selected few from the many which remain, and in which skin tests are of varying degrees of diagnostic value.

A. Dermatophytids and Moniliids.[4, 16, 17, 18]

Quantitative intradermal skin tests with trichophytin and oidiomycin and reading of the tuberculin type reaction forty-eight hours later are of only limited diagnostic value in adults. In cases of marked hypersensitivity, specific desensitization, while sometimes tedious and often difficult, can, however, generally be accomplished. In cases of true fungus "ids" this desensitization can lead to satisfactory results. In other "bacterids" the corresponding extracts should be employed.

B. Tuberculoderms.

Quantitative intradermal tests with dilutions of O.T. (Koch) ranging from 1:1,000,000 to 1:10 are of aid in the differential diagnosis of the various groups of tuberculoderms. These serve both for differentiation of various forms within the tuberculoderm group itself, and for their differentiation from dermatoses of other etiologies. The "contrast Moro" reaction, employed both on previously affected sites and on normal skin, with not only a tuberculin-containing ointment but also with a control blank salve, is often of greater diagnostic value than the intradermal test.[23, 24]

Specific desensitization can be accomplished and in some forms is of therapeutic value.

C. Lymphopathia venerea—including rectal strictures, ulcus vulvae elephantiasicum (esthiomène), etc.

Here the Frei test is pathognomonic, and treatment with Frei vaccine may be employed.[25, 26]

D. Soft chancre (chancroid).[4]

The Dmelcos vaccine (Ducrey bacilli) is of aid in diagnosis and treatment.

E. For all other uses of the skin test, including those in diphtheria, lues, pneumonia, and other infections, in parasitic infestations, etc.,

those interested are referred to the special literature and particularly to W. Jadassohn's treatise[4] on the immunbiology of the skin.

In closing, we should like to emphasize the fact that the most tedious and time-consuming but nevertheless most essential part of immunodermatologic-etiologic investigation lies not in the applying of skin tests, but in the establishment of the proper personal relation with the patient, and in the individually adapted manner of questioning. The first few interviews must often include pioneering and educational work. The patient must be convinced that what he thought was from "too much acid," "too rich food," or "thin blood," or "nerves," may really be caused by a tooth paste, or a face powder, a new plant, a fur coat, or by candy laxative or some such apparently incredibly simple and almost universally innocuous substance. Once the patient is convinced, he generally becomes the physician's assistant in the necessary detective work, and will bring, at each succeeding visit, new samples of substances which he suspects. These samples can often be applied directly to the skin as patch tests in the cases of contact type dermatitis or, in atopic and other dermatoses, can even be applied to scratches in the search for urticarial wheal sensitivity. We believe it worth mentioning again that the patient's understanding and cooperation are of primary importance in the search for causal allergens. In the average case it is, therefore, imperative for the physician to devote the often not inconsiderable time necessary for the patient's enlightenment.*

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THE PATCH TEST FOR GOLD HYPERSENSITIVITY*

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IN THE course of gold therapy for pulmonary tuberculosis and also in dermatological practice, skin lesions of various grades of severity have been reported frequently. Exfoliative dermatitis, sometimes fatal, has occurred. These reactions have generally been attributed to the toxicity of the gold preparation. That this explanation is not satisfactory is evident from the fact that severe reactions frequently follow the second or third dose, whereas other patients may tolerate many larger doses without mishap. The possibility of hypersensitivity to gold has been considered by some workers, but tests reported by two were negative.[1]

Studies carried out at the Municipal Tuberculosis Sanitarium of Chicago on a series of 102 patients over a period of a year have demonstrated that all patients who have skin complications give a positive patch test. Over 500 tests were performed.

METHOD OF STUDY

Several patients who had recovered from severe gold dermatitis were selected for preliminary study. Gold sodium thiosulphate in 30 per cent aqueous solution gave a positive vesiculative reaction on one patient. The same preparation, one third by weight in lanolin, gave positive tests on all the patients, and this form was used for all the tests which followed. Gold succinimid[3] put up in the same way was used as a control until it was found that no control was necessary. Later, patch tests with gold leaf, gold oxide, and gold succinimid were negative when made on a series of 10 patients. Gold chloride could not be used because of vesiculation of even the normal skin by the contained hydrochloric acid.

TECHNIC OF TESTING

Gold sodium thiosulphate (Abbott) or sanocrysin (Mollegaard) is mixed in the ratio of 1:2 by weight with lanolin. It turns yellow or brown with age but remains active indefinitely. The patient's arm is washed with ether, and an amount of the ointment the size of a split pea is rubbed gently on an area about 1 cm. in diameter. (A rubber finger cot should be used for handling the ointment.) The area is covered with several layers of gauze and a strip of adhesive tape, and read at forty-eight hours. Negative tests may show some brownish discoloration of the skin but no vesicles. Positive reactions consist of few

*From the Municipal Tuberculosis Sanitarium of Chicago.

or many pinpoint to pinhead sized vesicles on an erythematous base. These should be examined before washing the area because they are very superficial and are easily wiped away. Tests on a group of patients who received no gold therapy showed no positive reactions.

RESULTS

A group of 64 patients who had finished a course of gold therapy was first tested. The course consisted of weekly intravenous injections of sanocrysin or gold sodium thiosulphate (Abbott) from 0.1 gm. to 0.5 gm. until about five grams were given. Twenty-eight of this group gave positive skin tests. Of these, three had had exfoliative dermatitis, seven had milder skin rashes, three had severe neuritis, and five had severe gastrointestinal symptoms (sore mouth, anorexia, abdominal pain, and diarrhea). The remainder of the positive group had no observed complications. The 32 patients with negative tests had none of the above mentioned complications.

The next group tested consisted of 27 patients who were just commencing gold treatment. These were tested every week through the entire period of treatment. Ten patients developed positive patch tests, among whom four had severe dermatitis, two mild dermatitis, two neuritis, and one gastrointestinal disturbance. The positive patch tests appeared one to five weeks after the beginning of treatment. The complications began three to seven weeks after the beginning of treatment. The positive patch test usually preceded the onset of symptoms by one to three weeks.

A group of eleven patients who received treatment with gold succinimid instead of the thiosulphate compound was studied. Six were tested weekly for from ten to twenty weeks, the others at irregular intervals. The patch test with gold succinimid was invariably negative. Seven developed a positive patch test to the gold sodium thiosulphate preparation after a few weeks of treatment. One of this group had a mild dermatitis for two or three weeks.

In general it was noted that the most severe reactions occurred in those whose patch tests were most highly positive. Patients whose tests showed only one or a few vesicles usually developed mild if any complications.

A positive test once obtained on a patient tends to persist for a period of months, usually becoming weaker in time. Following subsidence of exfoliative dermatitis the four patients continued to give a positive test, the longest interval being two years.

In several patients it has been possible to continue gold therapy after subsidence of a mild or moderate dermatitis, although the patch test remains persistently positive.

No definite relationship appears to exist between the total quantity of gold administered and the duration of exfoliative dermatitis. Thus two

patients had total gold of 0.45 gram (in 3 injections) and 0.95 gram (in 6 injections), the acute symptoms lasting three and six weeks respectively. In two others who had 5 grams and 0.25 gram respectively the symptoms persisted several months. The intensity of the symptoms, however, was approximately the same in all four cases.

Examination of the weekly urinalysis records of the patients on gold therapy showed no correlation between hypersensitivity and kidney injury. Albuminuria occurred as frequently in the non-sensitive group as among those giving positive patch tests.

DISCUSSION

The findings in the series of cases investigated indicates that complications occur only in the hypersensitive group among those treated with gold compounds. The test for hypersensitivity is simple and can be repeated frequently, so that treatment can be stopped at once if one wishes to avoid complications. It is true that some of those giving a positive patch test never develop reactions, and most of the skin lesions are mild. Those patients who have exfoliative dermatitis, neuritis, and gastrointestinal reactions are made very ill, however.

That other factors or conditions besides hypersensitivity are necessary for the production of a rash is evident because some patients with positive patch tests do not develop a rash and, on the other hand, some who have had a rash and a positive test tolerate further treatment. Another paradox was noted in a patient who received 5 grams of gold, then developed a fixed area of dermatitis on the neck which persisted for six months. At this time an intravenous injection of sodium thiosulphate was given and was followed in six hours by generalized exfoliative dermatitis which lasted several months. The possibility that these variations depend upon the speed of disintegration of the gold compound in the body and the fixation or elimination of its products is being investigated. It may be that secondary chemical conditions in the body produce sudden mobilization of the fixed gold by a sort of trigger effect.

Complications were almost entirely absent among the group receiving gold succinimid, although many became sensitive. This may be attributed to the relatively slow rate of breaking down of this more stable compound within the body.

The experiments with various gold compounds indicate that the patients become sensitive to a particular gold ion (probably monovalent) rather than the whole compound. Patch tests are positive with the gold sodium thiosulphate alone, because this is the only compound tested which breaks down readily on contact with the skin to give such ions. Gold succinimid is too firmly bound to do this, so that it fails to give positive patch tests.

The fact that patients treated with gold succinimid give a patch test to gold sodium thiosulphate is of great significance in relation to other drug hypersensitivities. It emphasizes the necessity of testing the skin with the metabolic products of a drug rather than the whole compound. It may well be that herein lies the reason for the failure to demonstrate by skin test many drug hypersensitivities.

The type of hypersensitivity produced parallels closely that caused by the arsphenamine group. Intradermal tests and passive transfers were not attempted in the group studied here because of the necrotizing properties of the gold solutions. It is generally held that passive transfer is impossible in the arsphenamine hypersensitivity. No antibodies have been demonstrated to mediate the reaction.

About 50 per cent of the patients treated developed sensitivity. In contact dermatitis (rhus) it has been demonstrated that about 90 per cent of normal persons can be sensitized.

The skin rashes and gastrointestinal lesions produced are readily understood as evidence of surface reactions. The so-called neuritis is difficult to regard as a manifestation of hypersensitivity. Involvement of the nervous system in such reactions, however, has been experimentally produced and may depend upon the embryologic origin from ectoderm.

Exfoliation of the bronchial mucosa simulating bronchopneumonia was reported by Poole and Wehger[2] as the cause of death in cases of arsphenamine dermatitis. No similar effect was noted in the gold cases and no fatalities occurred.

The fact that albuminuria occurred as frequently among the nonsensitive as among the hypersensitive group seems to indicate that kidney injury is due to direct toxic action of the gold compounds.

CONCLUSIONS

1. Exfoliative dermatitis, rashes, gastrointestinal symptoms, and so-called neuritis among patients treated with gold compounds are due to the development of hypersensitivity.

2. The patch test with gold sodium thiosulphate 33 per cent in lanolin is positive in about 50 per cent of those treated, including all those who have the above complications, and persists over a long period of time.

3. The patch test, if performed frequently, will usually be found positive before complications occur.

4. Patients treated with gold succinimid become sensitive to the above mentioned patch test, but rarely show any complications.

5. Kidney injury cannot be correlated with hypersensitivity, but appears rather to be a direct toxic effect of the gold compounds.

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THE USE OF HOUSE DUST OIL AND THRASHER DUST OIL IN CONTACT DERMATITIS*

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IN A recent paper[1] the use of oil derived from house dust and thrasher dust was referred to as an adjunct in the diagnosis and treatment of certain patients suffering with contact dermatitis. In this paper a preliminary report of our studies will be given.

During the observation of several patients with a dermatitis which involved chiefly the exposed areas, it was noted that exacerbations occurred during periods of house cleaning, and at seasons when contact with house dust was increased. These patients were improved by hospitalization or by restriction of contact with house dust as a whole, but not necessarily by removal of suspected articles from the house. Several of them were tested with oils provided by the commercial laboratories, such as oil from orris, feathers, wool, etc., but showed no significant reactions. Some of them were tested with patch tests of the suspected dust with but slight reactions in two cases.

The idea occurred that perhaps the contact excitants of house dust could be concentrated or isolated. Accordingly, we attempted this by employing the same method used by Coca[2] in the extraction of the contact excitants from plants, etc. We were surprised to find a considerable yield of an oily gelatino-resinous material. Patch tests were applied routinely on suspected patients, as well as on normal people. Several patients showed reactions which simulated their original lesions. No normal people showed reactions, and many patients with atopic and contact dermatitis of known origin showed no positive reactions.

Three patients complained of increased itching while working around thrashing machines. Dusts brushed from thrashing machines were extracted, and the oil was used for patch tests. In each instance a positive reaction was obtained. The oils obtained from thrasher dust and house dust were diluted with almond oil. The various dilutions were sterilized by passage through a Seitz filter (gentle warming is sometimes necessary to obtain filtration), and treatment by injection of varying quantities of the oils has been instituted. Thus far, six patients have received house dust oil, and four have received thrasher dust oil, intramuscularly.

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Read before the Joint Meeting of The Society for the Study of Asthma and Allied Conditions and The Association for the Study of Allergy, Atlantic City, N. J., June 10 and 11, 1935.

I am unable to describe the appearance and clinical course of the patients who showed positive reactions to house dust and thrasher dust sufficiently to determine a clinical entity. It should be stated, however, that the appearance was that of an ordinary contact dermatitis. The history of exacerbations, when the patients were in contact with large quantities of dust, led us in many instances to predict positive reactions with patch tests.

The history of selected cases in which the patients have been treated by injections of house dust oil and thrasher dust oil will serve well to illustrate this point.

CASE REPORTS

P. O., a male, aged twenty-eight years, who lived in a basement, noticed a small patch of dermatitis on his ankle in 1931. He had been worse in cold weather and suspected that dust from the furnace caused an increase in itching. During a period when he worked as janitor in an apartment, he became much worse, and the dermatitis not only spread to his feet and legs but also involved his hands and forearms to the elbows.

He was tested by the patch method with many of the routine materials. Slightly positive reactions were noted to butesin picrate, Lifebuoy soap, sodium dichromate, nickel sulphate, an anilin dye, and a markedly positive reaction to house dust oil. A patch test with coal dust from around the furnace showed a slightly positive reaction, while a patch test with his own house dust showed no reaction.

On May 8, 1934, he was given the first injection of 0.2 c.c. of 0.5 per cent house dust oil. Injections were very gradually increased in amount and concentration at three-day intervals until on June 10 he received 1 c.c. of 1 per cent house dust oil. During this time he had improved greatly. At present, this patient has been symptom free for three months without injections. Recently a few small scaly areas have appeared on his arms, but no itching has been noted.

The patient has had patch tests with house dust oil several times during the course of the injections. The reactions have not decreased in intensity. When he was tested at first with ragweed oil, there was no reaction. Several months later a test applied with the same lot of ragweed oil showed a distinct but mildly positive one.

A patient whose case history was given in a previous report[1] has had a slight return of symptoms during this winter when windows have been closed, but symptoms have not been sufficiently severe to warrant treatment.

Three patients have been treated with thrasher dust oil, and observed until treatment was no longer necessary. One other who received thrasher dust oil did not return. Several other patients have shown re-

actions to thrasher dust oil. Many who had reactions to ragweed oil also reacted positively to thrasher dust oil.

One patient, L. T., a male, aged forty-eight years, showed a definite reaction to several plants. His history indicated that seven years previously he had an attack of poison ivy, which recurred each year in August; and in March, 1933, it became continuous. His longest period of freedom from symptoms since March, 1933 was three weeks. He knew that his condition was aggravated by being out of doors, and that he was definitely sensitive to ivy.

Patch tests with various plants in his immediate vicinity were made. He was found to react to ivy, leaf of giant and dwarf ragweed, and also to show a markedly positive reaction to thrasher dust oil.

On August 24, 1934, he had the first injection of thrasher dust oil. One week later he received 1 c.c. of a 1 per cent dilution which was repeated again in one week. By the tenth of September he was considerably improved. A patch test with dwarf ragweed applied at that time was markedly positive and resulted in a general exacerbation of his symptoms. At present, however, the patient is entirely well and has been so practically all winter. It is our plan to treat him with thrasher dust oil again this summer.

COMMENT

No specificity of house dust oil or thrasher dust oil is claimed. All patients who reacted to thrasher dust oil also reacted to ragweed, but not all who showed reactions to ragweed reacted to thrasher dust oil. It is possible that ragweed oil is one of the chief components of thrasher dust oil. A detailed study of the composition of thrasher dust oil is being undertaken.

One patient who reacted to house dust oil had a positive test to pyrethrum and ragweed oil, and one reacted to goat dander oil. Usually, tests with oils from component parts of house dust oil failed to give positive reactions in patients who reacted to whole dust oil.

The source of the house dust oil was not a factor which determined reactivity. It is believed that the use of house dust oil in diagnosis and treatment of certain types of contact dermatitis is of definite value in the relief of many patients who, perhaps, would be unable to obtain relief by other means.

NOTE: Since writing this paper, it has come to my attention that Sulzberger mentioned the use of house dust oil in testing patients with generalized neurodermatitis in a paper published in J. ALLERGY **3**: 423, 1932. No reference was found to its use in treatment and no further reference was found to its use as a diagnostic agent.

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PSYCHOGENIC URTICARIA

A Case Study

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THE following report of an individual with urticaria of two years' duration on a psychogenic basis is of special interest in that it represents the cooperative observations of dermatologist and psychiatrist. In a rather careful study of the literature in this field embracing both specialties, we are impressed with the fact that almost all reports are written either by a dermatologist with a conspicuous scotoma for the psychiatric point of view, or a psychiatrist who is likely to be equally blind to the dermatologic point of view. The dermatologists have reported the majority of studies of various types of dermatoses ascribed to psychologic factors. Unfortunately, most of these arrive at this etiologic conclusion through exclusion and propose to explain the origin of such neurodermatoses in such terms as "neurocirculatory instability" or "cutaneous masturbation." We feel that most value is to be obtained by a joint study of such cases by dermatologist and psychiatrist.

No reference is made here to the literature on psychologic factors in skin disease, in part because the literature is so extensive and in part because the subject has been reviewed recently by Stokes[1] from the dermatologist's viewpoint, and separately by K. A. Menninger[2] from the psychiatrist's viewpoint.

CASE REPORT

A young man, white, twenty-five years of age, came in requesting a Wassermann test of the blood because of a periodic itchy eruption appearing over his extremities when exposed to cold. The duration of the complaint had been two years.

History.—The patient was the second of seven children, all of whom are well. His father was forty-eight years of age, a janitor and music teacher, and was living and well. The mother died at the age of forty-two years of cancer within the abdomen, when the patient was fifteen years of age. There was no history of hay fever, asthma, urticaria, or other manifestations in any member of the family.

The patient was born in Canada, and lived there until seventeen years of age. The other siblings include a sister two years older than the patient, a sister three years younger, a brother five years younger, a sister seven years younger, a brother ten years younger, and a sister twelve years younger than the patient. The economic situation in the home had been only fair, but adequate during the patient's childhood, and he described the home life as congenial. He went through the grades and high school, and finished two years in the university, stopping at seventeen years of age because of family finances and especially because of his unhappiness at home with his stepmother. Following his mother's death, his father remarried against the patient's advice, within four months, and for the next two years the patient attempted to adjust to the new home arrangement. At seventeen years of age, he migrated to the United States to live with his older, now married, sister and her husband. He has resided now seven years with this sister and her husband in the States. For the last four and a half years, he has worked steadily for the same concern, a rug manufacturing house. His job has been one of assistant mechanical engineer, with some additional bookkeeping and accounting work. He does no hard labor. Prior to his illness, he had been fond of athletics and outdoor life, particularly swimming and hiking, and had always partaken of these activities frequently, both in Canada and since his residence in this country.

In the fall of 1932, he first developed the skin lesion of which he complains, a red, itchy rash, appearing over his limbs when exposed to cold or damp weather. The rash disappeared in warm temperature, and was entirely absent in the summer unless he would go swimming in cold water. The first appearance of the rash was not preceded by any physical illness; in fact, he has never had any serious illness.

During the two years' duration of this difficulty, it has never varied essentially from the same clinical picture. It has itched at times, but never severely. He had consulted several physicians, was given skin tests to which he feels he did not react; he was placed on special diets without effect, and regarded his medical aid as having been fruitless in giving him any relief. He had a tonsillectomy about two years ago, soon after the appearance of the rash, without effect on its manifestations. There was no history of venereal disease and previous blood Wassermann tests had been negative.

He described himself as being nervous, particularly so since this rash has been present. "My hands shake sometimes, and I am jumpy." He has quickly noticed any lack of his regular amount of sleep, and believed this has added to his nervousness. He frankly stated that he believed there was a relationship, not only between his nervousness

and the rash, but also between the rash and certain events that occurred in his life at the time of its appearance, as mentioned under the psychiatric note below.

Physical Examination.—On examination, the skin of the arms from the elbows down and from the middle third of the thigh to the feet was covered with grouped and solitary urticarial wheals, all of them about the same size: 1 cm. in diameter. His face was flushed, and there was moderate swelling around the eyes with edema of the lids and six or eight wheals on the forehead and cheeks. There was a rather marked dermatographia. The skin was otherwise entirely clear as were the scalp and mucous membranes. By the time the examination was completed the wheals and erythema were gone entirely.

It was thought that we were dealing with a case of allergy to cold but immersion of the forearms in a basin of cold water failed to reproduce the eruption. As the day was very cold the patient was instructed to dress and return to the office after a half hour's walk. When he returned he presented an eruption almost identical with the one noted at the beginning of his examination. His right arm was then immersed in very warm water to see if resolution of the wheals could be hastened. This produced no appreciable results. Thirty minutes after his return the skin was again entirely clear. Cold packs were then applied to the skin of the abdomen and chest which had not participated in the two attacks we had noted. This failed to produce other than a mild erythema. Except for the above, his physical examination, including dental, urologic, and nose and throat surveys, was entirely negative. A detailed examination by a competent allergist, a short time before his visit to us, was also negative. This examination included skin testing, intradermal or patch tests as indicated to numerous foods, articles of clothing, sweepings from his office and home, dyes, and other materials with which he came in contact while at his work. The patient refused to have these tests repeated because he had not experienced any relief during periods of absence simultaneously from both his home and his work.

The Wassermann and Kahn tests of the blood and urinalysis were negative. A gastric analysis was not insisted upon because of the entire absence of symptoms referable to the gastrointestinal tract.

The negative history and previous complete negative dermatologic examination, the inability to reproduce the eruption by the application of cold, its limitation to the arms, legs, and face (parts not covered by his bathing suit) when he went swimming in summer, its appearance after moving to a warmer climate and immediately after a severe psychologic upset, and the patient's nervous, apprehensive make-up, led us to believe that there was probably some psychologic factor influential in the eruption. This was revealed in the psychiatric examination, which follows:

Psychiatric Observations.—The patient was a quiet, reticent, noticeably passive individual. He told of his life freely, but rather hesitantly talked about what he felt were his inadequacies, his relations with women, the giving up of his masculine activities of sports and substituting sedentary and somewhat solitary interests.

The patient recalled no unusual events in his childhood which appeared significant to him. His father was a janitor in a school, but did some music teaching outside of his regular work. The father was described as having been a "good father" until his remarriage, since which time the patient had not communicated with him on account of differences with the stepmother. The patient's mother was the more stable individual of the two parents, and the patient described her as having been a quiet sort, "reliable and honest." He could recall no outstanding faults she had, and believed that he was her favorite child because "he was so easy to get along with." She was the manager of the family, taking over the family check and managing all money affairs. She was fond of her children, but not demonstrative toward them. The parents rarely had any quarrels and none of a serious nature.

Of the seven children, the patient was most attached to his brother five years younger and his sister seven years younger than himself, describing them as being the "most understanding." He got along well with his older sister, with whom he has lived for seven years, but was not attached to her.

He liked school and wanted to continue his studies in engineering. However, he was financially unable to do so, and the stepmother tried to dictate to him his hours of returning home at night, forbid his correspondence with the estranged older sister, select his companions for him, and other affairs; chiefly for this reason, he left his home. In school, he made only fair grades, but never failed. He took a very active part in athletics, playing on the university soccer and basket ball teams, and being especially interested in swimming and hockey.

In his religious life, he was a member of the Greek Orthodox church, and until he was seventeen years of age he was forced to go to confessions and take a part in the church life. He never believed in what he terms the "mysticism" of the church and ceased going to confession when he migrated to this country. He still attends mass, although chiefly because he sings in the choir.

He had been happy in the United States, and had been working steadily at his present job for about two years, when in January, 1932, he became interested in a girl. She was the first in whom he had ever had a "serious" interest, and for six months they had a happy enjoyment of each other. She, a girl of nineteen, was of Polish parentage and belonged to the Catholic church, and he is of Ukrainian extraction. He was affectionate toward the girl, but never had sexual

relations with her. He described himself as having been sexually aroused repeatedly by her embraces and was "annoyed" by his impulses, feeling he would be better off to be alone. Because of the racial differences, his sister and brother-in-law often urged him to forget this "foreign" girl, and the combination of these two factors made him decide to "forget" her, which he did with considerable emotional struggle. He now believes that his sexual continence, in the face of the repeated sexual excitement with this girl, is in some way responsible for his skin rash. He tried masturbating but with some mild sense of guilt attached to the act and without relief to his nervous or sexual tension.

He stated that being with this girl caused him to be up late at night quite frequently, and that the loss of sleep may have been a factor, since it was the first time in his life that he had lived so. He was apologetic for himself regarding his failure to have sexual relations with the girl, saying that "I just didn't make the right advance." He considered making the break with her for some two months before he came to a final decision; late in the summer of 1932, and when he did so, he described himself as being "quite upset" about it.

At the same time, his brother-in-law developed a peritonitis, and was not expected to live. "For the first time in my life, I was terribly worried. I had visions of taking on the support of his family and all the expense of his death. For three weeks we did not know whether he would live." And then the brother-in-law recovered.

Within the following month or six weeks, the rash first appeared on his heels while swimming, as a small area, and two weeks later following a second swimming party, it appeared over his entire body.

During the last two years, he has continued to have occasional dates with girls, but no steady companionship. He admitted no resentment toward his family, and expressed no regrets about having given up the girl. His sexual life has continued to bother him: he expressed a frank desire to have sexual relations with women but could not bring himself to make the approach, either to any girl with whom he kept company or to a professional. He said he did not know how to do it without insulting the girl. He has continued to go to mixed parties, likes to dance, but has had no further love affairs. At about fourteen or fifteen years of age, he began to masturbate, and did so at irregular intervals until he began going with this girl. During the six or eight months' association with her, he abstained, because "it would have been wrong." Suspecting some relationship between his rash and his dammed-up sexual outlet, he "experimented" by returning to masturbation for a period, without change in his feelings or the rash. About a year ago, he decided that masturbation was "contrary to nature" and stopped it, depending on his nocturnal emissions to relieve himself.

He talked frankly about the matter, and expressed no sense of guilt or wrong about his masturbation activities, insisting that he never had such feelings.

During the two years of the existence of the rash, his mode of life has changed in many ways. He occasionally played basket ball, but has entirely given up swimming, skating and outdoor activities except in summer, because these activities caused the "ugly" rash to appear. He has been more sensitive about his appearance than from the discomfort of the itchiness. He has gone out about twice a week with girls to parties or shows, spent two evenings a week with men friends, and spent the other time at home reading history and "business management." Formerly, he was interested in biography. He spent much time with engrossing as a hobby, a fancy lettering process. One evening each week he has attended faithfully the practice of the Ukrainian Chorus.

DISCUSSION

This presentation is unusual in that it represents the combined study and opinion of both the dermatologist and the psychiatrist.

From the data at hand, there is little doubt as to the psychogenic origin of this skin rash. That it does not arise from allergic causes, either physical or food, seems certain from the lack of a family history of allergy or previous allergic history in the patient, the sudden appearance of the rash at twenty-three years of age in apparent response to cold, in an individual who lived his first eighteen years in Manitoba, and showed no such reaction during four and a half years living in the same location in which his rash appeared.

The psychogenic factors are also obvious, though from the data at hand do not entirely explain this particular conversion symptom. His breaking of his first serious love affair within a month of the appearance of the rash, primarily because of his fears of sexual contact (i.e., unable to face the test of being a man) is of great importance in the etiology. This is followed immediately by a second psychic trauma in the fear that he might be called upon to support his sister's family, which is again a threat of necessity to prove his manhood, to which he reacted by violent nervousness and fear. Then he developed the rash, which again served to terminate his masculine activities of swimming and outdoor life, and substituted choral singing and fancy lettering. One can see obviously the purpose which the rash served his psychologic needs, i.e., made it possible for him to excuse himself from proving either to himself or the world his masculine character.

In part because of the secondary (unconscious) gain from the conversion symptom of his neurosis in solving his problem, and in part because of the reality factor of expense, the patient decided not to avail himself of psychotherapy. He readily accepted the interpreta-

tion given here and decided he "would try to work it through" by himself. In this connection, it should be pointed out that his rash has been present for two years, it has in no way affected his economic security, it causes him a minimal amount of actual physical distress, and he has accepted his present adjustment to life with little struggle and obvious satisfaction.

However, for the scientific interest as well as the relief of the psychoneurosis, it is unfortunate that the patient could not receive treatment. The psychologic function of the rash is reasonably clear, but its origin and psychologic significance remain in obscurity.

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MENNINGER CLINIC
159 NORTH DEARBORN STREET

DERMATITIS FROM PROPRIETARY HAIR TONIC

Search for Offending Ingredient by Patch Tests*

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INFLAMMATION from the use of proprietary hair tonics and other cosmetic aids to the hair, scalp and skin is encountered from time to time in dermatologic practice and in medicolegal work. What the percentage of cosmetic sensitized individuals may be is unknown at present. Certainly, only a very few persons can be sensitive to any popular brand of cosmetic, or very soon its sales would diminish. We have, for example, searched for a patient sensitive to lip stick application. We have found but one in an experience extending over at least ten years with no less than 5,000 new patients each year, of whom 60 per cent were women.

CASE REPORT

Mrs. R. C., aged forty years, born in the United States, reported to the out-patient department on May 10, 1932. She complained of a small lesion on the left side of the face which had been removed. Examination of the section microscopically revealed no malignancy.

The patient reported again to the clinic on Sept. 28, 1933. She related that she had applied a proprietary hair tonic and that an eruption had appeared. Her face was markedly swollen, and the skin of the forehead and other portions of the face was red and presented vesicles. A diagnosis of dermatitis venenata from the application of hair tonic was made. The conventional external remedies were applied. The patient was instructed to bring the bottle of hair tonic for further study. The eruption receded, and on her visit of Sept. 30, 1933, a patch test was made with a small portion of the contents of the bottle of hair tonic. The site of this patch test showed vesiculation and oozing resulting in a distinctly positive patch test.

The odor of the hair tonic recalled the odor of tar, and a patch test with an ointment of tar and zinc oxide was made on October 3. There was no local response to this application.

Our next efforts were to determine the portion of the hair tonic responsible for the irritation. With the active cooperation of the

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Research Laboratory of the hospital, the bottle of hair tonic was fractionated by distillation and condensation.

On October 17, a patch test was made on the right forearm with the black tarry residue after distilling the hair tonic. The skin at the site of this application responded with marked vesiculation and redness. On the same day a patch test was made on the left forearm with the condensation product of distillation coming over between 80° and 90° C. Although this gave a very distinct tarry odor, the result of the patch test was negative.

On October 31, 1933, further patch tests were made as follows:

Right forearm—Distillate—78°-79° C.—Negative result
80°-99° C.—Negative
Residue from alcohol solution of first residue.—Strongly positive (4 plus)

Left forearm—Distillate— 98° C.—Positive (2 plus)
101°-105° C.—Marked positive (3 plus)
120°-130° C.—Mild positive (1 plus)

The tarry residue from the distillation of the hair tonic which gave a strongly positive patch test on October 17 was dissolved in alcohol and the alcohol distilled off—the second residue was used in this patch test.

At 98° C. a fraction came over which smelled more of tar than the preceding portion from 80° to 98° C. The portion at 99° did not have this strong tar smell.

The distillate of the higher fractions condensed oil. The oil was removed and utilized in further patch tests as follows:

Left forearm (outer aspect)—
Oil from distillate—101°-105° C.—Marked positive (3 plus)
120°-130° C.—Positive (2 plus)
135°-140° C.—Marked positive

This oil had a foul odor as of rancid fat, which was very penetrating. Efforts made to identify the exact nature of the tarry residue were fruitless.

Further patch tests with tar products available in pharmacy, such as benzene, carbon tetrachloride, creosote, cresol, liquor pix carbonis, oil of birch tar, oil of cade, oil of pine tar, pix carbonis, pix pini, were negative.

SUMMARY

We report a clinical case of dermatitis venenata from the application of a popular high priced proprietary hair tonic. We have patch tested with the hair tonic, with a tarry residue after distillation, and with various fractions of the condensation products and of condensed oil. The results indicate that a quotient of the tar, not positively identified chemically, is responsible for the dermatitis in this patient.

The patient was not sensitive to the application of pharmaceutical tar in any form available in our hospital pharmacy.

18 East 89th Street

DRINKING WATER AS A CAUSE OF ECZEMA

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SINCE Watson and Kibler[1] reported a case of asthma which was proved to be due to drinking water, I have had a similar experience with a case of eczema which has proved to be primarily due to drinking water. Since the detailed history of this case is tedious and the protocols of laboratory tests and skin tests are extensive, an attempt will be made to present them in adequate summary only, giving only those details that seem pertinent to its understanding.

CASE REPORT

Miss M., white, aged nineteen years, was seen in June, 1932, suffering with a scaly, itching, eczematous eruption of both feet. This condition was so severe as to interfere seriously with usual activity. The eruption had appeared three years previously and had been diagnosed as a fungous infection by a competent dermatologist. Treatment at that time had cleared the condition fairly promptly, but within a few weeks it returned and had since been present. Its severity had varied considerably, occasionally clearing up almost completely. All manner of local treatment and x-ray therapy had been tried, some of which, for short periods, seemed to be of value. Always, however, within a short time the feet were in quite as bad condition as before. There had also been periods of improvement without relation to any treatment. The patient's past history was without significance. There had been the usual childhood diseases and a few minor illnesses, none of which seemed to be definitely allergic. The family history was, however, of importance. The mother suffered with asthma and one sister had hay fever.

Physical examination was essentially negative except for the eczema of the feet and some slight discoloration of the skin at the flexures of the elbows and over the popliteal spaces. On questioning, it was elicited that these areas occasionally presented a mild eczematous eruption, and that one such period had just passed. The usual laboratory procedures were negative at this time with the exception of an eosinophilia of 5 per cent. Repeated microscopic searches for fungi and cultures on Sabaraud's medium were negative.

It was assumed, due to the family history of allergy and the eosinophilia, that this was a possible case of atopic eczema, and that a careful search for the offending allergens and their removal would result

in freedom from symptoms. Accordingly a long series of skin tests was done for foods. It was realized, of course, that contacts were the most likely offenders; but as this phase had been experimented with previously without results, it was not studied again. Scratch tests were uniformly negative. A number of intradermal tests were positive, the most significant of which were wheat, milk, beef, asparagus, and several other vegetables. With these items as a basis, there followed a period of about eight months of trial dieting. There was considerable improvement, but there was never absolute clearing of the skin. There were no periods, however, that were so severe as to cause any considerable incapacity.

At this time, a patch test was done with a small portion of the leather from a pair of discarded shoes. There resulted a slight reaction which was considered doubtful. Patch tests were repeated with samples of different leathers secured from a shoe manufacturer. Several of these gave doubtful reactions after twenty-four hours' contact. One which remained negative was selected for use in the patient's shoes. Meanwhile a trial period of several weeks, during which shoes containing no leather were worn, resulted in some improvement. It had also been proved repeatedly that the ingestion of several of the foods which had been found positive resulted in exacerbations of the eczema as well as producing hives. At about this stage in the management of the case, a quite severe eruption appeared at the flexures of the elbow and rapidly involved the hands. Rechecks of the food tests gave no clue as to the cause of this new eruption. Contacts were studied with a wide variety of articles and materials from the patient's environment. All of these were negative. Basal metabolic rate now proved to be –19, and gastric analysis showed a low free hydrochloric acid concentration. Therapeutic trial on thyroid and hydrochloric acid did not influence the eczema, however.

At this juncture the patient took a vacation of two weeks in a nearby town. During this time, the eruption of both the hands and the feet cleared up entirely. Upon her return home, the eruption appeared again after forty-eight hours. There had been no dietary change during this vacation. This, of course, stimulated our search for a contact which might be responsible for the condition. Other patch tests were done with negative results. Then periods of avoidance of contact with various suspected articles were tried without results. Strongly suspected were articles and materials in a physician's office (her father's) where she worked. However, a six weeks' absence from the office, but not from her home, resulted in no improvement. Meanwhile, the eruption on the hands had become so severe that again she was seriously handicapped. During this time, almost two years, the patient and her father, a physician, had most faithfully followed directions and assisted in the search for causes. Many articles con-

tacted and suspected had from time to time proved to be of no significance. As a last resort, and because it was one of the items in the home environment which had not been duplicated during the vacation and which had not been ruled out as a factor, distilled water was substituted for the usual tap water for drinking and cooking. Within about five days practically all of the eruption has disappeared both from the hands and the feet, and in a few more days had entirely done so.

No further eruptions appeared for about three months, when the patient decided to substitute a so-called ultra pure deep well water, which was widely used for drinking as a substitute for the city tap water. Within forty-eight hours, the eruption had returned. Needless to say distilled water was promptly returned to with almost immediate relief. Since then, on one other occasion, tap water has been used for a short period when the supply of distilled water was unavoidably exhausted. There was also a return of symptoms then with relief as soon as distilled water became available.

There are many significant experiments that could be made to identify the factor in the water responsible for the findings in this case. Unfortunately, the patient resided in a town forty miles distant, and her visits to the office were infrequent, particularly after the condition subsided. As, more recently, she has married and moved to a still more distant town, it has been impossible to carry out any tests to determine what factor in the water was responsible. Nor is it by any means clear as to the mechanism whereby this factor caused the eczema. It is significant that the deep well water, which was not chlorinated and reputed to be exceptionally free of the heavy salt and mineral content of the waters of this region, caused the symptoms to return as promptly as did the tap water. It is impossible to say that this case represents an allergic reaction to some substance in the drinking water without further experimenting.

However, it is fairly definitely established that the drinking water acted as an etiologic factor in the eczema and from the practical standpoint might be considered as containing some true allergen.

SUMMARY

A case history is cited in which it seems fairly evident that the patient's drinking water contained some allergen or other substance which was the etiologic factor in a severe eczema.

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114 MILLS STREET

STUDIES IN ATMOSPHERIC POLLEN OF SAN FRANCISCO*

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WITH THE TECHNICAL ASSISTANCE OF BERNADETTE TILDEN, AND
ELSA BRUMLOP

OF THE many atmospheric pollen studies that have been published since 1916 only one[1] has appeared from the Pacific Coast. Even the recently published so-called national atmospheric pollen survey by Durham[2] failed to take into account much of the area west of the Rocky Mountains, and included only the period from July to November. It seems especially fitting, therefore, that some results of the studies in atmospheric pollen of San Francisco be permanently recorded and thus made available to all who are interested in the problems of pollen allergy.

To those of us who have studied the plants of California during the past twenty years and have compared the number of species yielding atmospheric pollen with the number found in other areas of equal size, it becomes apparent that California occupies a unique place. Jepson[3] has described 4,019 species of plants growing in California, of which 3,727 are native plants, while the remaining 292 are alien immigrants. To this list must be added the nearly 1,000 species of exotic trees, an equal number of exotic shrubs, and a much larger number of herbaceous perennials and annuals, making an approximate total of about 7,500 species of flowering plants. Of this number nearly one-half are wholly or partially wind pollinated. Studies of wind-borne pollen made between 1923 and 1933 in southern California and on the eastern shore of San Francisco Bay show that pollen counts in certain locations equal those of other parts of the United States. This is in contrast to what Durham[2] implies in his recent report.

Studies of the atmospheric pollen of San Francisco are of unusual interest because of the peculiar geographical location of the city and the existence within its limits of a large park containing nearly 900 species of trees and many species of grasses. An examination of the map in Fig. 1 shows that the city of San Francisco occupies all the area at the end of a peninsula bordered on the west by the Pacific Ocean, on the north by the waters of the Golden Gate passage, and on the east by San Francisco Bay. Since the direction of the prevailing winds is from west to east or from the ocean to the land mass, it would seem that the main source of atmospheric pollen in San Francisco must be the plants growing within

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the city limits. This we believe to be true to a large extent, but we cannot overlook, as a source of pollen, the plants growing on the mainland comprising the northern and eastern boundaries of San Francisco Bay. That these plants may be the source of pollen was suggested by an aeroplane trip over San Francisco and the ocean to the west in September, 1931. At that time coastal sage *(Artemisia californica)* was pollinating profusely in the Berkeley and Oakland hills on the mainland to the east. While traveling at an altitude of about 3,000 feet an odor of burnt sugar was detected, the source of which was traced to a sugar refinery about fifteen miles eastward. The wind at this elevation was blowing from east to west, i.e., from the mainland to the ocean. Two vaseline

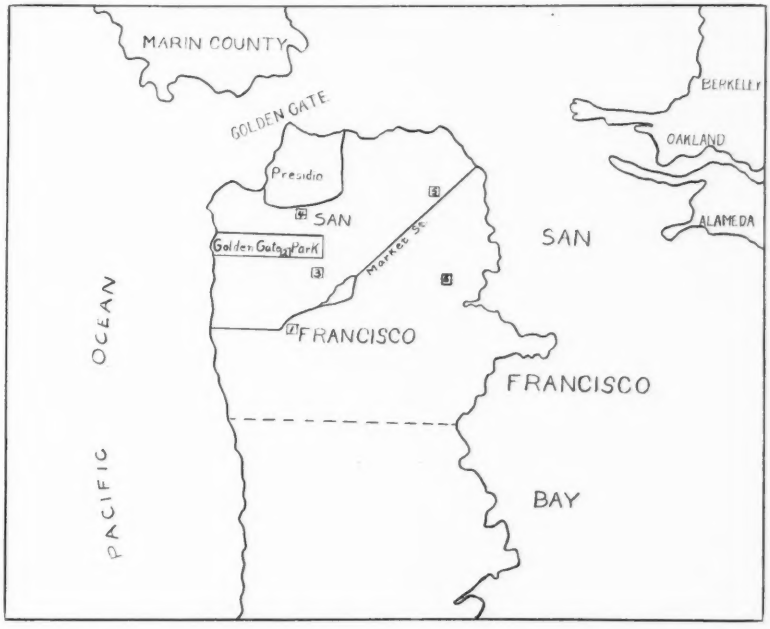

Fig. 1.—Map of San Francisco, showing the geographical location in relation to the adjacent land and water masses, and the location of the six pollen stations.

covered slides were exposed at this elevation and a microscopic examination showed the presence of pollen grains of *Artemisia californica,* probably originating in the Oakland hills. During the summer the winds at lower elevations occasionally blow from east to west and therefore would carry some pollen from the mainland to San Francisco.

The pollen counts were made from January, 1933, to January, 1934. Standard size microscope slides coated with a thin layer of vaseline were exposed daily at from four to six stations located in different parts of the city. The slides were placed horizontally under roofs of small tin shelters such as those used by Acquarone and Gay.[4] At approximately the same time each day the slides were taken in and new slides sub-

stituted. At the expiration of each week all slides were collected and sent to the laboratory for the identification and computation of the number of pollen grains.

The slides were examined with a compound binocular microscope fitted with 10x oculars and 16 mm. and 4 mm. objectives. All pollen grains observed in four 16 mm. objective views across the slide were recorded. Computations were made of the number of pollen grains of each species, or larger plant groups, which fell during twenty-four hours upon a square foot of surface. The area of one square foot was adopted in 1931 while one of the authors (H. E. M.) was making surveys in southern California in conjunction with Dr. George Piness. This unit area seemed more satisfactory of interpretation by the layman than 1.8 sq. cm., 0.5 sq. cm., and other areas used by different workers. It must be borne in mind by all who carry on and attempt to interpret pollen counts that all counts are subject to the greatest variation, due to local wind eddies, position of slides, amount of area actually observed in counting, etc. The general picture of atmospheric pollen in the various localities, however, can be sufficiently well "painted" by workers using different methods as to give a satisfactory indication of the yearly pollinating periods and relative abundance of pollen.

The identification of the pollens was made by use of the key and drawings published by Piness and McMinn,[5] numerous other published drawings and photomicrographs of pollen, and by comparison with pollen mounts. Tables I through VI show the results of the counts of the different stations.

Station I was located on a second-story window ledge of a residence in St. Francis Wood, which is a residential area of about 200 acres situated on a gentle sloping plain about two and one-half miles east of the western ocean boundary of San Francisco. The parkways and lawns of the entire area are planted with species of acacia, eucalyptus, pine, cypress, and other shade trees. The area between the ocean and St. Francis Wood is composed mostly of open fields and sand dunes partially grown over with several species of grasses and weeds yielding atmospheric pollen.

Station II was placed on the roof of one of the buildings of the California Academy of Sciences in Golden Gate Park. Nearly 900 species of trees grow in this park, and about 500 of these shed pollen which is wholly or partially wind blown. The extensive lawns in the park are sources of grass pollen.

Station III was located on the roof of the University of California Hospital, situated on the northern slope of a hill in a closely built-up residential area about three miles east of the western ocean boundary of the city and about four blocks south of Golden Gate Park. To the immediate south of the hospital is a forest of eucalyptus trees.

Station IV occupied a second-story window ledge of a flat located in the Richmond District, a closely built-up area without lawns or parkway

TABLE I—RECORD OF ATMOSPHERIC POLLEN FOR THE REGION OF ST. FRANCIS WOOD, SAN FRANCISCO, 1933, STATION I

COMMON NAME	BOTANICAL NAME	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.
Trees and Shrubs													
Acacia	Acacia	9 1 1	2	1 2 2	14 24 9	1	1	3 1 2	3 1 4 6	3 8 2 3	1 2 1	1 1	
Alder	Alnus		4 4 7 3	3 3									
Birch	Betula			2									
Hazel	Corylus		4 1										
Cypress family	Cupressaceae	6 1 4	52 3 27 24	3 1 2 3	7 33 17 88	83 34 29 78	38 50 31 127	179 139 173 12	4 9 7 7				
Eucalyptus	Eucalyptus	3 2 1 2	1 1	74 5 5	1 1 5 2	4 1 4 24	4 5 3 10	3 12 3 8	2 7	14 20	7 1 1		
Silk-tassel tree	Garrya												
Myrtle	Myrtus						5 14	38 38 91 158	24 39 61 82	16 22		1	
Pine family	Pinaceae		1 1	11 269 89 104	32 48 21 5	3 4 22	3 1 1 3	1 2 1	1 3 1	1			
Cottonwood	Populus		1 1	4 1 4 1									
Oak	Quercus			1	39 79 10 12	1							
Willow	Salix			1									
Elm	Ulmus			6 28	2								
Weeds													
Ragweed, etc.	Ambrosieae					1		1	1	1 9 1			
Sagebrush	Artemisia						1 3 5 3	5 3 9 1	25 28 4 6	1 1	1 1		
Amaranths, Chenopods, etc.	Amaranthaceae, Chenopodiaceae	1 1			1		1 6 5	19 10 8 9	8 3 7 3	1 1 1 1	1 1	1	
Plantain	Plantago				10 1	1 2	2 1 3	1 1 1					
Dock	Rumex				9 1 5	1 3 7 35	66 7 4 3	3 2					
Grasses													
Grass family	Gramineae	1 1			3 6 2 5	2 11 3 10	7 9 7 2	3 11 40	200 17 5	1 3 1			
Unknown		2 14	5 3 3	1 1 3	6 37 3	5 3 60	8 6 1 57	9	1 1 6	7 35 9	25 1 1	10 34	
Total		50	148	630	538	432	503	1,000	576	162	44	48	

NOTE—The numbers in the squares indicate the total number of pollen grains in terms of thousands which fell on an area of one square foot during a period of one week.

TABLE II—RECORD OF ATMOSPHERIC POLLEN FOR THE REGION OF GOLDEN GATE PARK, SAN FRANCISCO, 1933, STATION II

COMMON NAME	BOTANICAL NAME	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.
Trees and Shrubs													
Acacia	Acacia			1 1 1	1 1	1 1	1		1		1	1 7	
Alder	Alnus	1	1 5 12 1	3 2 1									
Birch	Betula			3	7 1								
Hazel	Corylus		1										
Cypress family	Cupressaceae	2 8 1	5 16 16 13	10 1 12 33	24 352 190 1363	892 1495 1227 5558	107 61 33 22	11 19 7 31	13 1 14 5	1 1		1 1	2 1 1
Eucalyptus	Eucalyptus	2 1 2 1	2	1 1	9 7 17 4	7 1 22 1	1 3 12	2 8 13 16	75 1 1 3	1 1 1	1 5	3 1	
Silk-tassel tree	Garrya		1 2										
Myrtle	Myrtus						9 3 1	2 3	36 1 3	3 9			1 1 1 1
Pine family	Pinaceae	1	1 1	25 177 493 195	68 109 94 135	18 9 10 21	5 3 3 1	1 5 1	2 2	1			1
Cottonwood	Populus			1 5 12									
Oak	Quercus			3 1	11 61 19 11	7 4 2 1							
Willow	Salix				12								
Elm	Ulmus			2 126 16	1								
Weeds													
Ragweed, etc.	Ambrosieae						1 3 1	1	1 3	3 1 1 1			
Sagebrush	Artemisia						23 4 2	5 41 22	15 1 7 2	5 1 5 5	5 3 8	1 2	
Amaranths, Chenopods, etc.	Amaranthaceae, Chenopodiaceae	1 2			1	1 4	3 2 4	7 12 13 16	7 5 12 1	1 1 3 4	4	1 1	
Plantain	Plantago				2 1 2	1 1 7	7 2 1 1						
Dock	Rumex				11 4 20	8 55 5 65	50 98 1						
Grasses													
Grass family	Gramineae	17 3	1	1	4 1 12 3	9 4 2 47	12 19 5 1	1 3 2	1 1 10	1 1	1 2	1	
Unknown		5 7 1		3 10 3 6	26 7 2 7	4 7 19 11	13 3 1	1 1 2	4 1 10 16	18 35 12 10	1 5 1 2	3 2 3 1	1 2 2 1
Total		55	78	1149	2600	9527	522	246	256	126	39	29	15

TABLE III—RECORD OF ATMOSPHERIC POLLEN FOR THE REGION OF UNIVERSITY OF CALIFORNIA HOSPITAL, SAN FRANCISCO, 1933, STATION III

COMMON NAME	BOTANICAL NAME	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.
Trees and Shrubs													
Acacia	Acacia			3	3 1 1				1				
Alder	Alnus	1 1	11 4 10 1	3 1 3									
Cypress family	Cupressaceae	11 1 5	62 11 14 22	4 1 1	35 24 32 49	76 85 43 37	11 12 24 22	13 49 20 12	7 14 7 1	1		1 4	2 1
Eucalyptus	Eucalyptus	13 1			1 2 2	4 1 2		2 1	1 1	1			
Myrtle	Myrtus							1 7	1	1			
Pine family	Pinaceae	1	1 3	9 26 141 33	46 37 31 26	5 7 1 50	8 5 1 1	4 2 9 1	8 2	1		1	
Cottonwood	Populus			1									
Oak	Quercus			1	49 91 15 3	1 2							
Elm	Ulmus			29 3	6								
Weeds													
Ragweed, etc.	Ambrosieae							1 1 1	2 9 16	2 1 1 8			
Sagebrush	Artemisia						3 1 3 12	4 11 33 8	11 6 9 2	2 2 1 2	5	4 3	1
Amaranths, Chenopods, etc	Amaranthaceae, Chenopodiaceae					1	3 1	4 5 10 5	4 15 2 3	3 3 1 3	2	1 1	
Plantain	Plantago				2	8		1 1					
Dock	Rumex				7 23 1 1	1 5 1 37		1					
Grasses													
Grass family	Gramineae		1	1	5 7 1 49	1 1 3 30	5 8 9 1	5 1 4	4 1 1 1	1 1 1			
Unknown		8 1 1	3 1	1 2 4	1 1 11	3 1 40		4 4 4 4	1 1 1 8	11 9 14 8	14 3 2 11	3 3 2 1	1
Total		44	144	267	563	446	130	233	140	78	37	24	5

trees. Pollens found on the slides from this station must have been blown from Golden Gate Park, the Presidio, and the vegetation of the sand dunes and vacant lots to the west.

Station V was located on a window ledge on the eighth floor of the Medico-Dental Building situated in the center of the main business district. Pollens found on the slides from this station were certainly blown in from outside districts.

TABLE IV—RECORD OF ATMOSPHERIC POLLEN FOR THE REGION OF THE RICHMOND DISTRICT, 1933, STATION IV

COMMON NAME	BOTANICAL NAME	JAN.	FEB.	MARCH	APRIL	MAY
Trees and Shrubs						
Acacia	Acacia		1	3 1 2 1	6 1 5 1	1 1
Maple	Acer				1 1	
Alder	Alnus		7 3 5 4	1 2		
Birch	Betula			1 1		
Hazel	Corylus			1		
Cypress family	Cupressaceae	1 3 4	47 20 14 32	6 3 2 4	44 85 46 171	179 89 93 40
Eucalyptus	Eucalyptus	1 1	1	2 2		7 2
Pine family	Pinaceae	1	3 1	4 105 55 35	23 24 10 20	5 5 1 37
Sycamore	Platamus			1 2	1 1 14	
Cottonwood	Populus			5 5		
Oak	Quercus				64 79 8 3	3
Elm	Ulmus			30 17	16	
Weeds						
Amaranths, Chenopods, etc.	Amaranthaceae, Chenopodiaceae	1 1 1		1	1 2 1	
Plantain	Plantago				1	5 14
Dock	Rumex					2 1 3 20
Grasses						
Grass family	Gramineae	1			2 2 3	7 3 10
Unknown		2 1 1	4 1	2 47 1 1	1 1 3 1	5 4 2 27
Total		19	143	343	642	567

Station VI was located on a window ledge on the top floor of the San Francisco Hospital situated in the Mission District. This district is composed of small apartment houses, two-family flats, and small business buildings closely built up. It is located about six miles from the ocean and one mile from the San Francisco Bay. Between the hospital and the ocean lies a range of high hills partially built up, but for the most part covered with grass and some planted trees. To the south lie low hills covered with grass and a few cultivated tracts which are always the source of some weeds belonging to the chenopod and amaranth families.

It does not seem advisable in this report to discuss the detailed results obtained from each station, but rather to give the general trend of the combined results of all stations. In this respect three points of general interest stand out: (1) The total pollen count of the air (exclusive of

TABLE V—RECORD OF ATMOSPHERIC POLLEN FOR THE MAIN BUSINESS DISTRICT, SAN FRANCISCO, 1933, STATION V

COMMON NAME	BOTANICAL NAME	JAN.	FEB.	MARCH	APRIL	MAY
Trees and Shrubs						
Acacia	Acacia	1			2	
Maple	Acer				1	
Alder	Alnus	1	7 7 5 1	1 3 12	1	
Birch	Betula				14 3	
Hazel	Corylus		1			
Cypress family	Cupressaceae	11 2 2	41 9 18 5	1 1 3	15 14 12 171	85 31 55 63
Eucalyptus	Eucalyptus			1	4	1
Pine family	Pinaceae		1	12 20 29 18	11 12 3 8	1 1 1 68
Cottonwood	Populus		1	7 1 7		
Oak	Quercus			1 4	57 51 7 16	2 3
Willow	Salix			1		
Elm	Ulmus			1 13 24	2 1	
Weeds						
Amaranths, Chenopods, etc.	Amaranthaceae, Chenopodiaceae	1			3 1	1
Plantain	Plantago					1 4
Dock	Rumex				1 3	5 6 28
Grasses						
Grass family	Gramineae	4	1		1 3 1 3	4 4 4
Unknown		1 7	1 2	1 5 1	4 5 3 3	1 1 14
Total		30	100	167	436	384

pollens from the pine and cypress families) is low compared to counts made by workers in the ragweed areas of central and eastern United States. (2) The pollinating seasons for the three main groups of wind pollinated plants, trees, grasses, and weeds, are much prolonged. (3) Tree pollen is relatively abundant and comes from nearly 500 species of trees, most of which have been introduced.

The average total pollen count per square foot for the year 1933 was 4,595,248. Of this number 3,173,000 pollen grains were from members of the pine and cypress families. The peak of the season occurred in May when an average total, from six stations, of 1,952,333 pollen grains was recorded for one square foot of surface. April ranked second with 838,000 pollen grains, and July third with 405,750 grains. For comparison with other areas Tables VII and VIII will be of interest.

It will be noted from Tables VII and VIII that Durham's ragweed count for Los Angeles in 1929 was much lower than that recorded by McMinn. Durham studied slides exposed at a single station located about ten stories above the street in the center of Los Angeles. McMinn's count was gathered from slides exposed at three stations located in different parts of the city and none higher than six stories. The low rag-

TABLE VI—RECORD OF ATMOSPHERIC POLLEN FOR THE REGION OF SAN FRANCISCO HOSPITAL IN THE MISSION DISTRICT, 1933, STATION VI

COMMON NAME	BOTANICAL NAME	JAN.	FEB.	MARCH	APRIL	MAY	JUNE	JULY	AUG.	SEPT.	OCT.	NOV.	DEC.
Trees and Shrubs													
Acacia	Acacia			1 1	1 1		1		1				
Maple	Acer			1									
Alder	Alnus	1	6 9 2 1	1 1									
Birch	Betula			1 1	2 1 1								
Cypress family	Cupressaceae	11 2 1	16 14 9 8	1 1	7 3 13 39	169 32 25 20	3 32 11 22	8 9 14 5	1 4 1 3	2 1		1	1 1
Eucalyptus	Eucalyptus	1 3			1	1	1 4	1 1 1	1 1				1
Myrtle	Myrtus												
Pine family	Pinaceae	1		1 64 32 9	6 15 11 3	5 1 3 16	2 11 3 3	1 3 3 1		1	1	1	
Cottonwood	Populus			2 3 1									
Oak	Quercus			1 1	45 39 8 7	4							
Elm	Ulmus			1 16 4	3 3								
Weeds													
Ragweed, etc.	Ambrosieae						1 5 1	3	1	1	1		
Sagebrush	Artemisia						3 12 12 6	5 2 1 10	1 5 6 1	1 2 1		3	1
Amaranths, Chenopods, etc.	Amaranthaceae, Chenopodiaceae	1				1 1	1 5 3 9	3 6 12 5	2 4 11 1	2 4	1		1
Plantain	Plantago				1 3 2	1	2						
Dock	Rumex				6 1 3	9 9 26	1 3 4	2 1					
Grasses													
Grass family	Gramineae	1			1 1 8	1 10 7	9 68 28 12	5 6 6 9	1 2 2 2	2	1		
Unknown		5 1	1 1	1 2 3 5	5 1 1 7	1 1 3 12	1 2 2	3 4 14	9 1 5	2 3 2 27	9 2 1 5	3 3 2	1 1 1
Total		28	67	155	149	358	283	144	66	51	21	13	8

weed count and the low total pollen count given by Durham for Sacramento is a surprise in the light of the abundance of vegetation found around that city.

A study of the records of the stations shows that grass pollen appeared on the slides during all months but December, and that the peak was reached in May and June, with one exception of a high count during one day in August. The grass count was lower than that found by one of us (H. E. M.) in southern California and in Oakland, California. The higher grass count found in southern California was due to Bermuda grass (*Cynodon dactylon*). This grass occurs very sparingly and sheds very little pollen in the cooler climate of San Francisco. The higher grass counts for Oakland were due to ray grasses (*Lolium multiflorum*

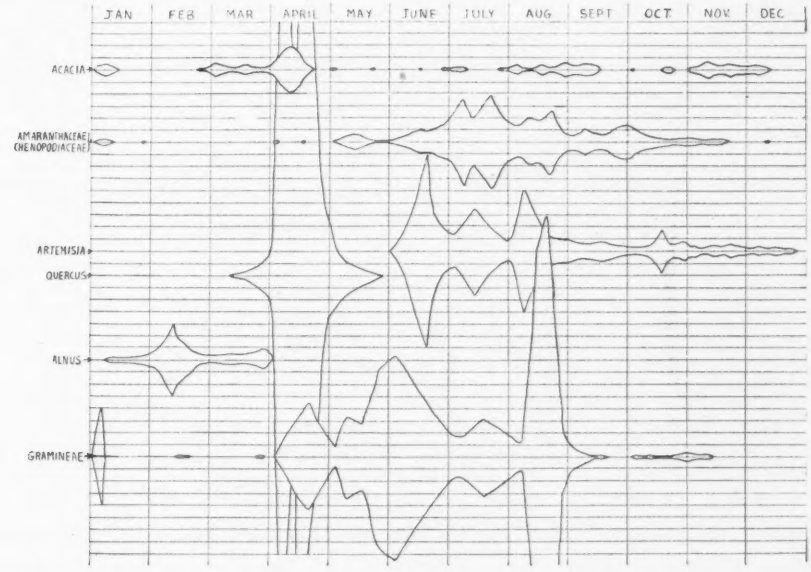

Fig. 2.—Record of atmospheric pollen in San Francisco during the year 1933. The spaces between the horizontal lines represent 500 pollen grains falling on an area of one square foot during twenty-four hours. The data used are averages of all stations.

and *L. perenne*). In San Francisco these grasses shed much less pollen than in the warmer parts of the state. The relation between temperature and amount of pollen produced by some species is a very critical one. Rattail Fescue (*Festuca myuros*) and foxtail barley (*Hordeum murinum*) occur in great abundance in vacant lots and semicultivated areas in San Francisco, but these species are notoriously poor pollen yielders. The twenty-four species of grasses which may be classed as potential causes of allergic manifestations in San Francisco do not shed as much pollen into the air as the two important grasses in the East, namely timothy (*Phleum pratense*) and Kentucky blue grass (*Poa pratensis*). Offsetting this lack of heavy production of grass pollen, however, is the very prolonged pollinating period.

Clinically, these observations have an important significance. With grass pollen present in the air during eleven months of the year the seasonal nature of a patient's symptoms, caused by grass pollen, is largely obliterated. The determination of a specific grass pollen as the offending

TABLE VII

TOTAL POLLEN PER SQUARE FOOT FOR JULY, AUGUST, AND SEPTEMBER

CITY	SEASON	POLLEN GRAINS
Chicago	Average 1932-1933 (Durham)	3,489,192
Indianapolis	Average 1932-1933 (Durham)	9,680,160
Los Angeles	1933 (Durham)	211,560
Los Angeles	1929 (McMinn)	799,791
Sacramento	1933 (Durham)	152,736
San Francisco	1933 (Deamer and McMinn)	769,500
Washington, D. C.	Average 1932-1933 (Durham)	1,143,972
Whittier, Calif.	1929 (McMinn)	570,157

(NOTE:—In making pollen counts Durham used an area of 1.8 sq. cm. Since we used an area of one square foot, it was necessary for comparison to convert Durham's metric units into English equivalents.)

TABLE VIII

TOTAL POLLEN FROM THE RAGWEED TRIBE (AMBROSIEAE) FOR THE ENTIRE SEASON

CITY	SEASON	POLLEN GRAINS PER SQ. FOOT
Chicago	Average 1929-1933 (Durham)	2,627,988
Indianapolis	Average 1929-1933 (Durham)	6,745,668
Los Angeles	1929 (Durham, 1 station)	16,512
Los Angeles	1929 (McMinn, 3 stations)	169,059
Los Angeles	1933 (Durham)	74,304
Sacramento	1933 (Durham)	17,544
San Francisco	1933 (Deamer and McMinn, 4 stations)	86,000
Washington, D. C.	Average 1929-1933 (Durham)	1,162,548
Whittier, Calif.	1929 (McMinn)	151,123

substance is rendered very difficult because there are at least twenty-four possible offenders to consider. Here it is not possible simply to diagnose timothy sensitivity with symptoms from May 23 to July 20, as is the case in the East. While Coca, Walzer and Thommen,[6] and Stull, Cooke and Barnard[7] believe there is but one antigenic substance in grasses, common to them all, this has not been the experience of Piness and Miller.[8] Some workers even feel that it is necessary to treat a patient with almost all the different grasses to which he gives a positive skin test and with which he comes in contact. We feel that this question is still open for further careful observation. That the grasses have some antigenic properties in common is, however, fairly generally accepted. It is suggested by the almost identical appearance of their pollen grains, and demonstrated by the frequent occurrence of a general grass sensitivity in a patient to the exclusion of almost everything else. Such patients give positive skin tests to all of the twenty-four grasses to which we test them, and either no other reactions or a few scattered positive reactions among trees and weeds. Occasionally,

however, the opposite is true, and definite reactions are obtained to scattered individual grasses, the rest being negative.

Pollens from the order Chenopodiales (Chenopodiaceae and Amaranthaceae) were found on the slides during eleven months of the year. The peak of the season was reached during June, July, and August. During these months several species of chenopods (*Chenopodium*), saltbushes (*Atriplex*), amaranths (*Amaranthus*), pickle weed (*Salicornia*), sea blite (*Suaeda*), and *Roubieva* were in flower. Pollens from the ragweed tribe (Ambrosiae) of the sunflower family (Compositae) appeared in small numbers from the last week in May to the first week in October. These pollens probably came from false ragweeds (*Franseria chamissonis, F. bipinnatifida*), Clotbur (*Xanthium spinosum*), cocklebur (*Xanthium canadense*), and western ragweed (*Ambrosia psilostachya*). One other group of clinical importance, usually classed as weeds, is the sagebrush or mugwort (*Artemisia*) group. Three species of *Artemisia* occur in San Francisco, and their pollens appeared on the slides from the first week in June to the last week in November. Field sagewort (*Artemisia pycnocephala*) occurs on the sand dunes and vacant lots in the western part of the city. It flowers from May to September and produces abundant pollen. Mugwort (*Artemisia vulgaris* var. *heterophylla*) flowers from July to October and coastal sage (*Artemisia californica*) flowers from August to November. These two species grow more abundantly in the ravines and on hill slopes in the southern part of the city. Other weed pollens appearing on the slides were plantain (*Plantago*) and dock (*Rumex*), but these give very few clinical reactions.

The largest amounts of pollen found on the slides came from trees. This is not particularly surprising when one realizes that there are, as has been previously stated, nearly 900 species of trees in Golden Gate Park, an area consisting of 1,013 acres. By far the greatest amount of the tree pollen came from members of the pine (Pinaceae) and cypress (Cupressaceae) families. A total of 128 species of trees in Golden Gate Park belong to these two families, but, since their pollens have not been proved to cause allergic symptoms, they may be left out of the picture as far as clinical diagnoses are concerned. So inactive is pine pollen that Peshkin[9] uses it as a control in dry pollen ophthalmic tests. He has never obtained, as far as we can ascertain, a positive test with pine pollen. Phillips[10] in Arizona states that, although pine pollen is abundant in the forests of Arizona, no one at the resorts has symptoms from it, and that many sufferers from pollinosis go to these forests for relief. A few species of "cedar" (*Juniperus virginiana, J. sabinoides, J. pachyphloea, J. scopulorum, J. utahensis*) seem to be outstanding exceptions and have been reported to cause trouble occasionally.

Pollen from eucalypti and acacias was found on the slides from all the stations during the twelve months of the year, but was more abundant from the stations located in St. Francis Wood, Golden Gate Park, and

at the University of California Hospital. About 90 species of the genus *Eucalyptus* and over 50 species of the genus *Acacia* grow in San Francisco. The pollens of all the species of eucalypti examined were triangular in shape and had retusely truncated corners; therefore the identification of the species from the pollens on the slides was impossible. All the species of acacias have almost spherical pollen grains, sculptured on their surfaces with patterns of concentric polygons.

Very little is known regarding the allergic properties of acacia and eucalyptus pollens. Statements made by patients, however, not infrequently incriminate acacia. Eucalyptus is much less frequently suspected by them. It seems probable that even though the two were of equal allergic potency, acacia because of its more showy flowers would draw more attention. If we grant a fairly close relationship between skin tests and clinical sensitivity in the pollen groups, some light may be shed on the question. In a group of 100 patients for whom pollen treatment sets had been prepared, 9 patients (9 per cent) had significant positive scratch tests to acacia. Sixty-six of this group of 100 had been tested with eucalyptus pollen and four gave significant scratch tests (6 per cent). Rowe[11] has stated that severe symptoms may be due to acacia pollen, including asthma, hay fever, dermatitis, and pollen toxemia. He also reports positive skin tests with eucalyptus pollen on a number of patients, and believes that it probably causes some allergic symptoms. Alderson[12] reports that over a period of six years' testing with acacia pollen he has seen only a few mild skin reactions and no constitutional reactions. From these observations it seems reasonable to conclude that sensitivity to acacia and to eucalyptus does occur and may require treatment. We are inclined to believe, however, that usually they are of minor importance.

Other tree and shrub pollens found on the slides came from species of oaks (*Quercus*), elms (*Ulmus*), maples (*Acer*), alders (*Alnus*), hazelnut (*Corylus*), birches (*Betula*), silk-tassel bush (*Garrya*), *Myrtus*, sycamore (*Platanus*), cottonwood (*Populus*), and willow (*Salix*). Only oak and alder pollens were found in significant amounts. Most of these trees have short and rather clear-cut pollinating seasons, thus differing from acacia and eucalyptus.

SUMMARY

1. Although it is recognized that pollens may be carried great distances by the wind, it is our opinion that the bulk of the atmospheric pollen in San Francisco has as its source plants growing within the confines of the city. We believe this is due to the peculiar geographic location of San Francisco and to the direction of the prevailing winds.

2. The total pollen content of the air in San Francisco (exclusive of pollen from members of the pine and cypress families) is low compared to that of the ragweed areas of central and eastern United States, but

is as high as the counts made by us in other California cities and much higher than those made by Durham for Sacramento and Los Angeles.

3. In San Francisco tree pollens are very abundant. They come from a wide range of species, and they extend over a wide seasonal range.

4. Eucalyptus with about 90 species and acacia with over 50 species present problems needing further study.

The authors wish to express their appreciation to Miss Evelyn Graham for assistance in the identification of pollens and in preparation of the charts, and to Miss Mary Lake and Miss Jean Kingston for statistical assistance.

This study was aided by a grant from the Christine Breon Fund for Medical Research.

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A BOTANICAL SURVEY OF NORTHWESTERN CALIFORNIA

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THE area included in this report forms a natural geologic unit dominated by the Coast Range and Klamath Mountains, which form the eastern boundary. The height of the mountain barrier on the east averages about 6,000 feet in the Klamath Mountain Range and about 4,000 feet in the Coast Range toward the southern end. The southernmost 50 miles of the eastern boundary have no mountain barrier. The western boundary is the Pacific Ocean. Although the survey concerns counties in California only, the plants common to Del Norte County will be found as far north as the Rogue River in southern Oregon, which constitutes a natural boundary to the floral region studied. The southern boundary is the San Pablo Bay and to the west of the San Pablo Bay the range of mountains dominated by Mount Tamalpais. The whole area is an uplifted ocean plain which has been dissected by river erosion into valleys and low mountain ranges.

The climate of the area can be considered under two headings. The coastal area is dominated by the ocean winds and hence has a very moderate climate with fogs and daily sea winds. Heavy rains fall during the winter. The average rainfall in the northern part is 80 inches, while the lowest precipitation in the coastal section is 20 inches at Fort Bragg. The maximum summer temperatures of the littoral districts range from 95° F. at Crescent City, which is protected by a headland, to 75° F. at Eureka, which receives many cooling summer fogs. In winter the temperatures fall as low as 26° F. around some of the sheltered inlets during short cold snaps. The winds blow from the north except in the very southern portion where the prevailing winds come from the northwest.

The inland valleys constitute a second large climatic area. The regions are protected from the ameliorating influence of the ocean by mountain ranges to the west. The extremes of temperature in this section show a wider variation as compared with the coastal section. The summer temperatures often reach 105° F., and the winter temperatures as low as 20° F. The prevailing winds are from the south with local convectional winds through the summer.

The Eel River valleys have north and northwest prevailing winds during the summer. These bring in the heavy ocean fogs which regulate the temperatures. These fogs which have a vertical thickness from 1,000 to 3,000 feet are believed to limit the areas where the redwood tree can grow.

The population distribution of the area is important from the standpoint of pollinosis. The total area of the region studied is 13,030 square miles, in which reside a total of 138,935 people according to 1930 census.

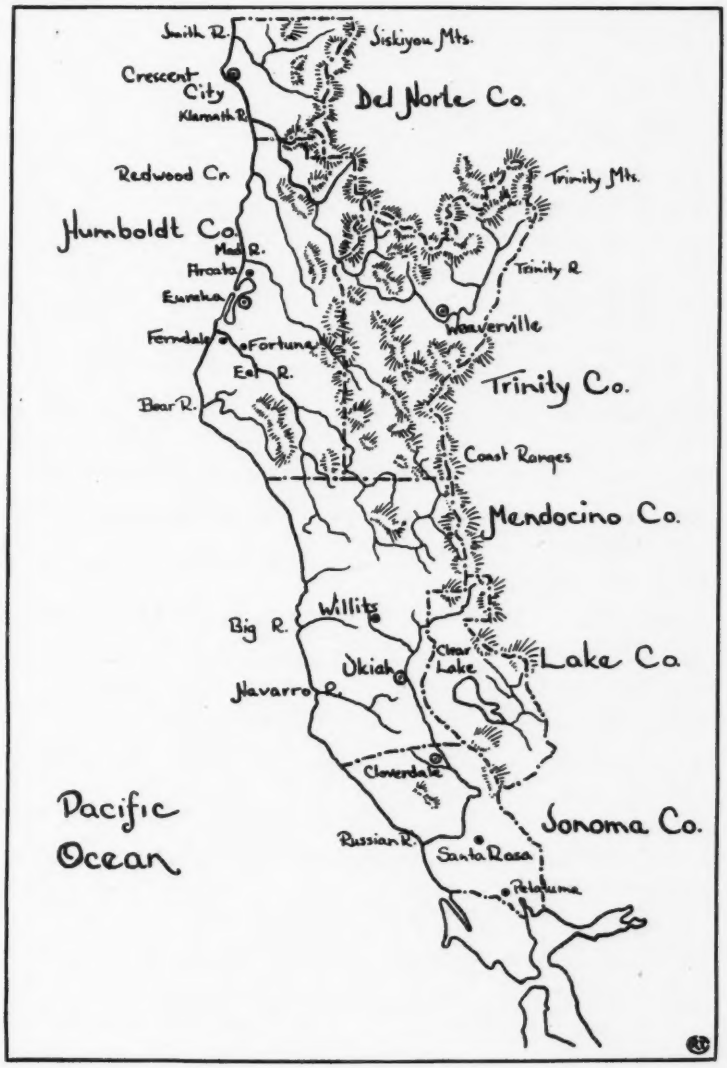


Fig. 1.

Most of the people live in the valley lands along the rivers and around the Humboldt Bay. The population density per square mile is as follows:

	PERSONS PER SQ. MILE		PERSONS PER SQ. MILE
Del Norte County	1.0	Mendecino County	6.64
Humboldt County	12.09	Lake County	5.78
Trinity County	0.91	Sonoma County	39.34

TABLE I

BOTANICAL SURVEY OF NORTHWESTERN CALIFORNIA

NOMENCLATURE	DURATION OF SEASON *												DISTRIBUTION BY COUNTY †					
	1	2	3	4	5	6	7	8	9	10	11	12	D. N.	HUM.	TRIN.	MEND.	LAKE	SONOMA
Festuceae																		
Briza major				//	////	//							1CV	2CVF	2VF	2CVF	2VF	2CVF
(Quaking grass)													1CV	2CVF	1VF	3VF	3VF	3CVF
Bromus carnatus					//	////	////	/										
(California Brome grass)													1VF	2VF	2VF	2VF	2VF	2VF
Bromus hordeus					//	////	//											
(Soft cheat)																1CV	3VF	3C2VF
Bromus maritimus					////	////	///											
(Seaside Brome grass)																2V	2V1F	3V1F
Bromus rubens				////	////	////	/											
(Foxtail Brome)																2V	2V	2V
Bromus unaloides				//	////	////												
(Rescue grass)																3V	4V	4V
Dactylis glomerata					/	////	////	//										
(Orchard grass)													3C	3C		3C		3C
Distichlis spicata				////	////	////	///											
(Salt grass)													2VF	2VF	2VF	3VF	3VF	3VF
Festuca reflexa					////	////												
(Few flowered fescue)																2VF1C	3VF	2VF1C
Melica torreyana				////	////	//												
(Torrey's melica)																	2VF	2VF
Melica imperfecta			///	////	////	/												
(Small flowered melica)													4CVF	4CVF	3VFM	2VF	2VF	1VF
Elysmus Glaucus					/	////	////	//					2M	2M				
(Western rye grass)																		

* Horizontal numbers 1 to 12 refer to months of year; vertical lines indicate the number of weeks.

† D. N., Del Norte County; Hum., Humboldt County; Trin., Trinity County; Mend., Mendocino County; Lake, Lake County; Sonoma, Sonoma County. C, Coastal region; V, inland valley region; F, inland valley and protected coastal region; M, mountainous regions. Numerals mean: 1, rare; 2, moderately common; 3, common; 4, abundant.

Hordeae																	
Hordeum murinum						////	////	////					4CVF	4CVF	4VF	4CVF	4VF	4CVF
(Foxtail)																		
Hordeum sativum				/	////	////	////	///					1CVF	2VF	2VF	3CVF	4VF	4VF
(Cultivated barley)																		
Lolium perene			///	////	////	////	////	///					3CVF	3CVF	2VF	3CVF	3VF	3CVF
(Eng. rye grass)																		
Aveneae																		
Aspris carophylla													2CVF	2CVF	2VF	2CVF	2VF	2CVF
(Silvery hair grass)					//	////	////	/					1M	1M		1M		
Avena fatua													3CVF	3CVF	3VF	4CVFM	4VFM	4CVFM
(Wild oats)			///	////	////	////	////	//										
Avena sativa					//	////	////	/					2CV	2CV	2VF	3CVF	4VF	4CVF
(Cult. oats)																1M	2M	4M
Notholcus lanatus						//	////	////					2CV	3CVF	3VF	4CVF	4VF	4CVF
(Velvet grass)														2M	1M	3M	3M	4M
Agrostideae																		
Agrostis verticillata						/	////	///					—	2CV	—	3CVF	4VFM	4CVF
(Bent grass)																		4M
Agrostis maritima								////	////	/			3CV	3CV	—	3CV	—	3CV
(Maritime bent)																		
Agrostis palustris					/	////	////	////	////	/			3CV	3CV	—	3CV	4VF	4CV
(Red top)													1FM	1FM				4FM
Ammophila arenaria						//	////	////	//				2C	2C	—	2C	—	2C
(Beach grass)																		
Stipa lemmonia							////	////					—	1V	1V	3VF	3VF	3VF
(Lemmon's needle)																		
Chlorideae																		
Cynodon dactylon							////	////	///				—	—	—	2VF	3VF	3VF
(Bermuda grass)																		
Phalarideae																		
Phalaris californica					//	////	////	////	////				—	1VFM	1FVM	3VFM	3VFM	3VFM
(Canary grass)																		

TABLE I—Continued

BOTANICAL SURVEY OF NORTHWESTERN CALIFORNIA

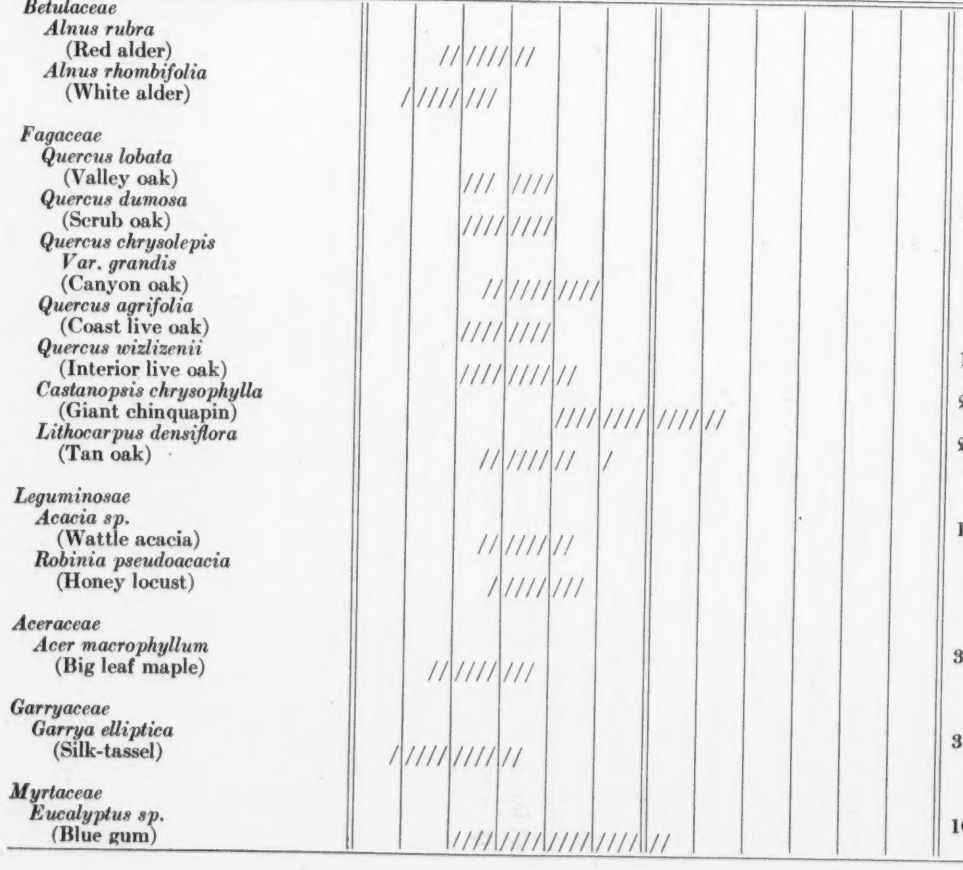
NOMENCLATURE	DURATION OF SEASON *												DISTRIBUTION BY COUNTY †					
	1	2	3	4	5	6	7	8	9	10	11	12	D. N.	HUM.	TRIN.	MEND.	LAKE	SONOMA
Oryzeae																		
Zea Mays (Indian corn)					///	////	////	//					2CVF	2CVF	1VF	3CVF	3VF	3CVF
HERBS																		
Urticaceae																		
Urtica gracilis (Hoary nettle)							////	////	///				2CVF	2CVF	2VF	2VF	2VF	3VF
Urtica californica (California nettle)						////	////	////					2CV	2CV	—	2CV	2V	2CV
Polygonaceae																		
Rumex occidentalis (Western dock)			//	////	////	////	//						3CV	3CVF	2VF	3CVF	2VF	4CVF
Rumex crispis (Curly dock)			//	////	////	////	//						2CV	2CVF	2VF	2CVF	2VF	2CVF
Rumex conglomerata (Green dock)			//	////	////	////	//						1CV	2CV	1VC	2CV	2VF ICV	2CV
Rumex pulcher (Fiddle dock)			//	////	////	////	//						2CV	2CV	1V	2CV	1V	2CV
Rumex acetosella (Sheep sorrel)			//	////	////	////	//						3CVF	4CV 3F	3V 2F	4CVF	4VF	4CVF
Chenopodiaceae																		
Chenopodium album (White pigweed)			///	////	////	////	////	///					3CV	3CVF	3VF	3VFC	3VF	3CVF
Chenopodium carinatum (Pigweed)				////	////	////	////						1CFV	2CVF	1VF	2CVF	2VF	2CVF
Atriplex patula (Spear orache)						//	////	////	///				2C	2C		2C		2C

Chenopodiaceae—Continued																	
Atriplex hastata												2C	2C		2C		2C
(Fat hen)																	
Atriplex Californica												2C	2C		2C		2C
Atriplex Leucophylla						////	////	////	////			4C	4C		4C		4C
Salicornia ambigua					////	////	////	///				4C	4C		4C		4C
(Pickle weed)					//	////	////	////	//								
Amaranthaceae																	
Amaranthus retroflexis												3CVF	3CVF	2VF	3CVF	2VF	3CVF
(Rough pigweed)					· //	////	////	////	//								
COMPOSITAE																	
Ambrosiae																	
Ambrosia psilostachys												3CVF	3CVF	2VF	3CVF	2VF	3CVF
(Western ragweed)							////	////	////								
Franseria bipinnatifida												3CVF	3CVF	2VF	3CVF	2VF	3CVF
Franseria chammissonis					/	////	////	////	///			2CV	2CV	1V	2CV	1VF	2CV
(False ragweed)					/	////	////	////	///								
Xanthium spinosum												1CV	2CV	1V	2CV	2V	2CV
(Spiny clotbur)													1F		1F		
Xanthium canadense												2CVF	2CVF	2VF	2CVF	2V	2CVF
(Cocklebur)				/	////	////	////										
Anthemidae																	
Artemesia pycnocephala												3C	3C		3C		3C
(Sagebrush)							////	////	////			1VF	2VF		2VF		2VF
Artemesia californica												2CVF	2CVF	1VF	3CV	3VF	3CV
(California sagebrush)						////	////	////							2FM	2M	2FM
Artemesia vulgaris												3CVF	3CVF	3VF	3CVF	3VF	3CV
Var. heterophylla															1M	2M	2FM
(California mugwort)						//	////	////	//								

TABLE I—Continued

BOTANICAL SURVEY OF NORTHWESTERN CALIFORNIA

NOMENCLATURE	DURATION OF SEASON *												DISTRIBUTION BY COUNTY †					
	1	2	3	4	5	6	7	8	9	10	11	12	D. N.	HUM.	TRIN.	MEND.	LAKE	SONOMA
Pinaceae																		
Pinus contorta (Beach pine)			////	////	////								2C	2C		2C		
Pinus radiata (Monterey pine)			////	////	////								1V	2CV		2CV	2VF	2CVF
Picea sitchensis (Sitka spruce)		/	////	////	////								3C	3C	1V	2C		
Tsuga heterophylla (Western hemlock)			///	////	////	/							3C	3CV		2C		1C
Pseudotsuga taxifolia (Douglas fir)		////	////	////	////								4CVF	4CVF	3VFM	3VF	1M	2FM
Abies grandis (Lowland fir)			////	////									2C	2C		2C		
Taxodiaceae																		
Sequoia sempervierns (Redwood)	/	////	////	////									3CVF	4CV		2CV		2CV
Thuja plicata (Canoe cedar)			/	////	///								2V	2V	1V	1V		
Cuppressus macrocarpa (Monterey cypress)			///	////	////								1CV	2CV	1V	2CV	2V	2CVF
Chamaecyparis lawsoniana (Lawson cypress)				//	////	///							2V	2V	2V	1V		
Salicaceae																		
Salix sitchensis (Sitka willow)		///	////	////	///								3CVF	3CVF		2CVF	1V	2CVF
Salix piperia (Dune willow)		/	////	////	/								3C	2C		1C		
Populus trichocarpa (Black cottonwood)		/	////	/									2CVF	2CVF	2VF	2VF	2VF	2VF



Betulaceae																	
Alnus rubra (Red alder)													4CVF	4CVF	1VF	2CVF	
Alnus rhombifolia (White alder)													1CVF	2CVF	1VF	2CVF	3VF
Fagaceae																	
Quercus lobata (Valley oak)														1VF	2VF	3VF	3VF
Quercus dumosa (Scrub oak)													1FM	2FM	3FM	2VFM	3VFM
Quercus chrysolepis Var. grandis (Canyon oak)														1F	2F	2F	2F
Quercus agrifolia (Coast live oak)																	2VF
Quercus wizlizenii (Interior live oak)													1VF	2VF	2VF	2VF	2VF
Castanopsis chrysophylla (Giant chinquapin)													2FM	2FM	2FM	2FM	2FM
Lithocarpus densiflora (Tan oak)													2VF	3VFM	4VFM	4VFM	2VFM
Leguminosae																	
Acacia sp. (Wattle acacia)													1V	2V		2VF	2VF
Robinia pseudoacacia (Honey locust)																2VF	2VF
Aceraceae																	
Acer macrophyllum (Big leaf maple)													3VF	3VF	2VF	2VF	
Garryaceae																	
Garrya elliptica (Silk-tassel)													3CV	3CV		3CV	
Myrtaceae																	
Eucalyptus sp. (Blue gum)													1CV	2V	1V	2CVF	3CVF

Betulaceae	
Alnus rubra (Red alder)	2CVF
Alnus rhombifolia (White alder)	3CVFM
Fagaceae	
Quercus lobata (Valley oak)	3VF
Quercus dumosa (Scrub oak)	3VFM
Quercus chrysolepis Var. grandis (Canyon oak)	2F
Quercus agrifolia (Coast live oak)	2VF
Quercus wizlizenii (Interior live oak)	2VF
Castanopsis chrysophylla (Giant chinquapin)	2FM
Lithocarpus densiflora (Tan oak)	2VFM
Leguminosae	
Acacia sp. (Wattle acacia)	2VF
Robinia pseudoacacia (Honey locust)	2VF
Aceraceae	
Acer macrophyllum (Big leaf maple)	
Garryaceae	
Garrya elliptica (Silk-tassel)	3CV
Myrtaceae	
Eucalyptus sp. (Blue gum)	3CVF

Pollen production starts early in the winter, with heavy amounts from certain of the conifers. The pollen showers increase in abundance until about May as the grasses and shrubs come into bloom. The pollen production then decreases until October when the fall rains clear the air.

Conifers produce all their pollens during the late winter and early spring. Some catkins remain in bloom during the summer, liberating small amounts until the fall rains come.

The deciduous trees produce their pollens during the early spring when the winds are blowing. The earliest of the pollens is liberated about the first week in March and the last in August. Most of the trees, however, finish blooming about the latter part of May.

Grasses produce most of their pollen during late spring and through the summer. By May nearly all of them have started to flower and have completed their flowering by the latter part of July. The grasses are most abundant in the Russian River valleys, around Clear Lake, and in Sonoma County. Along the river valleys of the north many of the coastal grasses and herbs have migrated inland, establishing themselves on cutover land.

Weeds and shrubs tend to produce their pollen during the latter part of the spring and during the summer. Since they grow slowly as compared with the grasses and are easily affected by seasonal variations in temperature and rainfall, their pollination varies according to rain and temperature. The largest number of species are in bloom in June and July with many continuing into August. The marshes which bound the inlets and embayments yield large amounts of Salicornia pollen. The river bars and flats support large growths of ragweed, while the open or bald places on the hills often are densely covered with sagebrush. In the redwood belt the sheep sorrel (*Rumex acetosella*) is a very common garden pest, as it grows very well in soil which is slightly acid. The season for this plant is frequently extended by warm weather during the Indian summer.

Certain trees included in the report do not come under the heading of forest trees. Along the coastal bluffs in the north, specimens of *Garrya elliptica* are commonly found. The acacia and eucalyptus trees are popular windbreaks and shade trees in most of the area. In the warmer valleys the locust is a commonly used street tree. These trees usually bloom in the late spring or early summer.

SUMMARY

1. The area studied includes the counties of Del Norte, Humboldt, Trinity, Mendocino, Lake, and Sonoma, all of which are coastal counties of northwestern California lying on the western slope of the Coast Range Mountains.

2. These counties have a total population of 138,935, which is largely concentrated in three of them.

3. The flora of the northern section of the area is dominated by a heavy coniferous forest in which there are few grasses, with the exception of cutover areas. The central and southern part of the heavily populated district includes river-bottom land and inland valleys on which grasses and oaks predominate. The inlets and marshy areas adjacent to the ocean support large growths of Salicornia.

4. The important regions from the viewpoint of the number of pollen-producing plants are the Humboldt Bay littoral, the Russian River Valley, and the plains about Clear Lake.

5. The largest number of plants which produce wind-borne pollen are in bloom during the late spring and early summer, at which times the coastal section has prevailing north winds originating over the ocean, while the valleys and Lake County have valley winds from the south and local convectional winds.

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Reports of U. S. Weather Bureau.

DEATH FROM TEN GRAINS OF ASPIRIN*

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GENERALIZED reactions following the ingestion of aspirin are by no means uncommon, manifesting themselves by more or less generalized urticaria, nausea and vomiting, asthma, or by some combination of all of these. Death resulting from aspirin sensitiveness is apparently relatively rare. Cases ending in death have been reported by Dysart,[1] and by Lawson and Thomas.[2]

CASE REPORT

W. R., male, aged twenty-seven years, Italian. At the age of twenty-four years following a severe cough for four months the patient gradually began to have dyspnea of the asthmatic type. Thereafter there was scarcely a day when he was free from dyspnea. In the last year of his life he required from 2 to 8 doses of epinephrine daily.

The patient appeared in the allergy clinic of the Rochester General Hospital in May, 1931, and was seen there at intervals until a week before his death in February, 1934. Skin tests with the inhalants, foods, etc., were negative. Several operations for the removal of nasal polyps were performed. The maxillary antrums were washed out on one occasion. The washings contained a small amount of purulent material. Further surgical procedures on the sinuses were advocated but the patient refused. When the nasal polyps were first removed, there was slight temporary relief from the asthma.

Treatment with autogenous and stock vaccines, potassium iodide, and a variety of cough medicines produced no benefit. A member of the patient's family was instructed in the use of a hypodermic syringe and administered epinephrine whenever necessary.

In September, 1931, the patient was given 5 grains of aspirin for severe headache. One-half hour later he was brought to the emergency department of the hospital suffering from an extremely severe attack of asthma for which he needed epinephrine in doses of 10 minims repeated four times in two hours. He was hospitalized four days. At this time he volunteered the information that he had had one similar but milder attack of asthma after taking aspirin one year previously. A skin test with aspirin done at this time was negative.

*From the Allergy Clinic of the Rochester General Hospital and the Medical Service of the Genesee Hospital.

On February 4, 1934, the patient appeared in the emergency room of the Genesee Hospital where he had never been before, complaining of severe asthma. Physical examination showed a small emaciated man who was extremely dyspneic; blood pressure 124/70 mm. Hg; pulse 120 per minute; temperature 99° rectally. There were no physical findings of importance except those related to the respiratory apparatus. His nose was moderately obstructed by swollen mucous membrane. The chest was distended and moved but little on respiration. The percussion note was hyperresonant throughout. Expiration was prolonged, and there were many coarse râles and whistling rhonchi. The heart was not enlarged, and the heart sounds were normal.

The patient was given 15 minims of epinephrine subcutaneously, 3/8 grain of ephedrine sulphate, and 3/4 grain of amytal by mouth. His asthma was considerably relieved by medication, but he still appeared so sick that he was admitted to the ward. He complained of very severe headache and was given 10 grains of acetylsalicylic acid. One-half hour later he became very excited, his asthma became much worse, and he then stated that he was sensitive to aspirin and had previously suffered severe reactions from it. Immediately after this he went into collapse. He became very cyanotic, the pulse was weak and thready, and respirations were gasping with periods of apnea lasting several seconds. He was given 7½ grains of caffeine sodium benzoate, and 15 minims of epinephrine. Oxygen was given by nasal catheter. The blood pressure after his collapse was unreadable. After about one-half hour the respirations gradually became of the asthmatic type. His pulse was 112 per minute; his blood pressure rose to 160/120 mm. Hg, but he never regained consciousness. Thirty hours later the patient died.

*Autopsy Finding.**—The principal points of interest in the autopsy were findings in the lungs and in the brain. The pia arachnoid was edematous and the blood vessels were congested. All the ventricles of the brain seemed normal, but the capillaries of the roof of the fourth ventricle were congested causing general reddening of this tissue. Sections through the cerebral hemispheres showed evidence of moderate congestion. The thorax was moderately rounded out laterally and anteroposteriorly. When the thorax was opened, the lungs were found fully distended and did not collapse. Filliform adhesions bound the visceral and parietal pleura loosely together. There was no fluid in the pleural sacs. The left lung weighed 330 grams and the right 440 grams. Although the dependent parts were somewhat darker red than the rest of the lung, they remained crepitant on palpation. Sections through the freshly cut lungs were cream and pink in color. There were no masses, cavities, or pneumonic consolidations. The

*The autopsy was performed by Dr. Herbert Brown.

mucosa of the bronchi and bronchioles was moderately congested and coated with rather tenacious mucus.

The heart was small, weighed 250 grams, and was normal in outline. The myocardium was normal in thickness. The endocardium and valves were normal in appearance. The coronary vessels were patent and of normal size. The stomach and intestines were normal. The liver was normal in appearance as were the pancreas and kidneys. The spleen was slightly enlarged, but otherwise appeared normal.

COMMENT

This patient had had two previous episodes of severe asthma and prostration following the ingestion of small doses of aspirin. It seems probable that the summation of the effects of the severe asthmatic attack for the treatment of which he applied at the Genesee Hospital, and the reaction to the ingested aspirin, were necessary to produce death.

REFERENCES

1. Dysart, B. R.: J. A. M. A. **101**: 446, 1933.
2. Lawson, R. W., and Thomas, Roy: J. A. M. A. **99**: 107, 1932.

A NEW METHOD FOR COVERING PILLOWS

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THE various methods used for covering pillows and hair mattresses have proved unsatisfactory with many patients suffering from asthma, vasomotor rhinitis, etc. Some patients have complained of the expense entailed in using oiled silk; others have objected to the odor and discomfort of oilcloth; while still others have found rubber sheeting far from a good substitute for the ticking ordinarily covering pillow and mattress.

In looking about for some way to overcome these obstacles, Mr. John Coleman, chemical engineer of this city, directed my attention to a process which is quite simple, inexpensive, and apparently efficient as regards completely sealing in the contents of both pillow and hair mattress. So far no patients using these processed articles have developed symptoms which previously resulted from contact with them. The product used is a liquid rubber or latex, which is painted on the outside of the pillow or mattress with an ordinary paintbrush. When first applying the latex it has much the same appearance as white paint, and an ammoniacal odor; but upon drying, it is odorless and leaves a glazed and transparent surface. One side of the object is painted at a time and allowed to dry for about one-half hour, following which the surface so treated is rubbed with talcum powder in order to remove the mildly sticky surface which remains. The opposite side of the object is then treated in a similar manner and the pillow or mattress is ready for use. As will be explained later, no vulcanizing is necessary. The material so treated is thoroughly impregnated with the liquid, and the seams are well filled in. After a brush is used for applying latex, it should be immediately washed in running water and then in benzol. This chemical is an excellent rubber solvent and satisfactorily removes the small rubber particles which collect on the brush when drying. It is a good plan to put the brush in benzol when not in use, just as one uses turpentine for the ordinary paintbrush.

Latex is on the market under various trade names. The particular product used in the above mentioned process is called Vultex, Grade F487.*

As is generally known, rubber is produced from a juice obtained from the bark of the rubber tree. As it runs from the tree it has the appear-

*Vultex is made by the Vultex Chemical Company, 666 Main Street, Cambridge, Mass. The price is very reasonable, and one pint of material will ordinarily process two pillows of average size.

ance of milk, and is known as rubber milk or liquid latex. In preparing rubber this latex is coagulated with acids or other chemicals, sheeted, washed, and dried. This ordinary rubber of commerce when received by the manufacturer must be masticated between huge rolls and compounded, and vulcanizing ingredients must be added. It is then remilled and dissolved in solvents, or passed through still heavier calenders before it is ready for use. The next step is vulcanization. This is usually accomplished by the incorporation of sulphur and accelerators with the rubber, and the application of various degrees of heat to the finished product. The use of prevulcanized latex products such as Vultex eliminates these costly intermediate processes. The latex is brought to America in its liquid form and by various patented processes is prepared for use in its original liquid form. This is accomplished by prevulcanizing the particles of rubber as they are suspended in the liquid rubber milk or latex, without coagulating the rubber. The resulting vulcanized latex does not differ materially in appearance from the original latex, but when dried it immediately becomes a finished vulcanized product, thus eliminating the laborious and expensive preparatory and after-vulcanization to which articles made from ordinary rubber must be subjected. Tests also demonstrate that liquid vulcanized latex products stand exposure to sunlight, oils, oxidation, and detrimental influences to a much greater degree than when ordinary rubber is used. The use of costly solvents is also avoided, thus eliminating the destructive residue which sometimes follows such use.

Department of Reviews and Abstracts

Selected Abstracts

Anaphylactogenic Properties of Milk. Immunochemistry of the Purified Proteins and Antigenic Changes Resulting from Heat and Acidification. Ratner, Bret, and Gruehl, H. L.: Am. J. Dis. Child. **49**: 287, 1935.

Hypersensitivity to milk is a relatively common cause of food allergy. These authors undertook to examine what antigenic changes result when cow's milk is boiled, evaporated, superheated, dried, or acidified, to explain if and why there is a greater tolerance of milks so modified in hypersensitive individuals.

Guinea pigs were the experimental animals and the anaphylaxis method was employed; sensitization and shock were induced both by parenteral injection and by oral administration of the antigen. Standard products widely used for infant feeding were used for comparison.

Because they were able to show that the proteins isolated from raw milk are chemically and biologically distinct, these authors stress the importance of using highly purified proteins showing that it is impossible to draw any valid conclusions where the protein fractions are obtained from crude separations of the casein and whey.

From their experimental data, Ratner and Gruehl conclude that no antigenic changes, either of the whey or casein fractions, result from the drying, acidification or pasteurization of milk.

As a sensitizing agent, given by injection, milk which is evaporated, freshly boiled for several hours, or superheated, shows practically no loss of the antigenic character of the lactalbumin. As a shock agent, given by injection, evaporated or superheated milk shows an unmistakable loss of the antigenic properties of the whey fraction. This is more marked with evaporated than with superheated milk (Smaco 303). Superheated and evaporated milks show no loss of the antigenic properties of the casein fraction. From their clinical observations and a review of the literature these authors are forced to the conclusion that more individuals are hypersensitive, and sensitive to a more marked degree, to the whey fractions than to the casein fractions of milk.

Evaporated, freshly boiled, and acidified evaporated milks, when fed by mouth, show a marked reduction in sensitizing ability. Coagulation delays the passage of the proteins through the gastrointestinal

tract, making for more complete digestion, and thereby diminishes the possibility of the absorption of native antigens through the intestinal wall.

One may therefore conclude that evaporated milk can be taken with impunity by persons markedly sensitive to the whey fractions of milk.

Anaphylactogenic Properties of Malted Sugars and Corn Syrup. Ratner, Bret, and Gruehl, H. L.: Am. J. Dis. Child. **49**: 307, 1935.

It has generally been held that only such food substances as contain protein constituents are capable of producing those altered reactions in man which are grouped under the common term allergy. However, there has recently appeared a preparation of dextrimaltose sugar which purports to be nonallergic. The question, therefore, has been raised as to whether food substances so widely used in infant feeding and ordinarily designated as carbohydrates may give rise to exacerbations in the allergic person. The substances most commonly used in infant feeding, and which were investigated, are standard preparations of malt extracts, of dextrimaltose, and of corn syrup.

The experimental work was carried on in the guinea pig and immunologic methods were used. From their experimental evidence, Ratner and Gruehl conclude that malt extracts and the barley malt from which they are derived are highly anaphylactogenic; they react specifically to the original protein constituent present in barley, hordein. Persons who are sensitive to barley may show allergic symptoms after the ingestion of malt extracts and malt brews.

The experiments reported make it apparent that pure dextrimaltose, corn syrup, and crystalline sugars, because of the processes to which they are subjected, are nonanaphylactogenic and play no rôle in allergy.

The addition of wheat germ or dried milk to nonanaphylactogenic preparations of dextrimaltose converts them into substances which are definitely anaphylactogenic and may produce allergic exacerbations in persons sensitive to wheat, yeast, or milk. Allergy to carbohydrate foods cannot, therefore, be attributed to the carbohydrates per se but must be ascribed to the protein constituents which are added to certain compound carbohydrate food preparations.

The Polypeptan Treatment of Alimentary Idiosyncrasies. Urbach, E.: Wien. klin. Wchnschr. **48**: 213, 1935.

The author has devised a new propeptan preparation which contains 12 different specific foodstuffs, as lamb, beef, pork, egg, milk, potatoes, spinach, peas, etc., in amounts of 25 mg. each. One or two of these tablets taken three-quarters of an hour before meals, on an empty stomach, permits one eventually to eat the above foods without difficulty. After some three weeks of such treatment, offending foods

can usually be tolerated. If not, allergy has evidently become established, and one either omits the offending food or uses the specific propeptan and not the mixture for the purpose of alimentary desensitization.

The Pathogenesis of Diffuse Glomerulonephritis as an Allergic Disease of the Kidney. Masugi, M.: Klin. Wchnschr. **14**: 382, 1935.

The author reviews his extensive experimental work on diffuse glomerulonephritis produced in rabbits by administration of rabbit kidney antiserum obtained from ducks. The writer believes that the diffuse glomerulonephritis is a result of an antibody-antigen reaction affecting the capillary system in the glomerulus. The clinical picture is characterized by albuminuria, hematuria, cylindruria, lipoid droplets in the urine, hypertension, increased nonprotein-nitrogen fraction, edema, and death from renal insufficiency. The anatomical pathologic picture is characteristic of, and identical with, the pathologic picture observed in human cases. In certain cases it is possible to produce experimentally what was considered to be typical periarteritis nodosa.

This report is of interest as it reviews work published in Japanese journals.

The Effect of Phenol in Hyperesthetic Rhinitis with Tissue Study of the Nasal Mucosa. Palmer, A.: Ann. Otol. Rhin. and Laryng. **44**: 25, 1935.

Thirty consecutive cases of hyperesthetic rhinitis were treated with phenol. A thorough application of concentrated phenol, U. S. P., was made to the entire nasal mucosa, excepting the olfactory area. In some cases an application of 2 per cent to 5 per cent cocaine solution was made prior to treatment. Vaseline and alcohol were used to protect the vestibule and the mucocutaneous margins of the nose, and care was exercised to avoid the nasopharynx. In 6 cases a second application was made. All other therapeutic measures were omitted. The immediate effect was coagulation followed by an acute edema and obstruction and hypersecretion. There was a sense of stuffiness, heaviness in the head or headache. The clogging lasted twenty-four to forty-eight hours, followed by slough.

Of the 30 cases, 24 showed definite improvement and 12 were free from symptoms from one to nine months. Sections of the mucous membranes were examined before and after treatment. Microscopically, there was less edema after phenol application, but an increase in connective tissue.

It is concluded that the application of phenol to the nasal mucosa in cases of hyperesthetic rhinitis is of value in both the seasonal and perennial types.

Experiences in Ionization of the Nasal Mucous Membrane. Tobey, H. C.: Ann. Otol. Rhin. & Laryng. **44**: 95, 1935.

Sixteen patients, eight with hay fever, and eight with vasomotor rhinitis, were treated with nasal ionization by the usual technic. Relief from hay fever was secured if ionization was done during the season. Although relief was obtained in 85 per cent of the cases, it is concluded that whereas the immediate results of vasomotor rhinitis were excellent, desensitization should be the method of choice in hay fever.

Parallergy. Moro, E., and Keller, W.: Klin. Wchnschr. **14**: 1, 1935.

Parallergy is a term proposed by the authors in 1926 to designate the changes in the reactivity of previously tuberculin negative children after vaccination with smallpox vaccine. The previously negative tuberculin reaction becomes positive when the reaction due to the vaccination has reached its maximum. This parallergic sensitivity to tuberculin disappears after ten days or two weeks. A similar parallergic tuberculin sensitivity can be observed during the serum sickness due to the injection of horse serum. The allergic manifestations resulting from the administration of the horse serum will be specific, while the parallergic reaction, of course, is not specific. Positive parallergic Dick and Schick reactions following vaccination have been observed.

The angina occurring after vaccination is also considered to be parallergic in nature. The cases of encephalitis after vaccination are, at least in a certain percentage, considered to be parallergic, notwithstanding the possibility that the vaccination virus might cause such an encephalitis. The writers further consider the possibility that encephalomyelitic reactions during measles and the angina preceding measles might be parallergic in nature. They mention that although Wallgren considers erythema nodosum as possibly parallergic in nature, this hypothesis can explain only a certain percentage of cases with erythema nodosum. Moro and Keller have pointed out that they have seen erythema nodosum in children with definitely negative tuberculin reactions.

The phlyctenule is usually considered to be a manifestation directly due to or accompanying tuberculosis. However, Moro and Keller state that phlyctenules have been known to occur in children (approximately 4 per cent) with entirely negative tuberculin reactions, for instance during pertussis, during the course of epidemic influenza, in a patient during convalescence from rheumatic polyarthritis, and after serum injections.

Of special interest is a case reported by W. Freund, quoted by Moro and Keller, in which a child known to be tuberculin negative before

and after allergic manifestations to cow's milk, had a definite and repeated positive tuberculin reaction while the allergic manifestations to cow's milk were exhibited.

Moro finally offers the following tentative definition of parallergy: "We call parallergy a change in reactivity of the organism against nonspecific irritants, organic or nonorganic in nature, different from the primary antigen which has induced the specific allergy. Parallergy is a condition facultatively accompanying allergy which manifests itself mostly as an increased and more rarely so, as a decreased inflammatory reactivity. It is transitory in nature, is most pronounced during the time of development and fluctuation of the allergy, and may become manifest during stationary allergy."

Fatal Asthma. Report of Case with Bronchial Measurements. Bubert, H. M., and Warner, C. G.: J. A. M. A. **104**: 1469, 1935.

A woman of sixty-nine years, with no family history of allergy, but a past history of skin rash from definite food ingestion, developed symptoms of asthma one year or two years before admission, which gradually became more severe. Examination revealed asthmatic breathing and emphysema. The blood pressure was 178/88 mm. Repeated sputum examination revealed no spirals or eosinophiles, which was explained by possible faulty technic. There was no blood eosinophilia. The asthma progressed while the patient was in the hospital and she apparently succumbed to it, as no other mechanism was found to explain death. On postmortem, both lungs were emphysematous. Histologic study of the bronchi revealed the usual characteristics of allergic asthma. Of significance was a study of bronchial measurements taken at various levels according to the method of Hüber and Koessler, which confirms previous investigations in that the musculature of the bronchi was found to be thickened when compared to normal controls.

Autohemotherapy in the Treatment of Bronchial Asthma. Maddox, K., and Back, R.: M. J. Australia **1**: 277, 1935.

Ten cubic centimeters of blood taken from the median basilic vein were immediately injected into the buttock. There were five such treatments at weekly intervals. Treatment was quite successful in children, of whom there were twenty-four less than sixteen years of age. The good results in this group are attributed to the fact that asthma is more apt to be purely allergic and less complicated. Results were better in the first decade than in the second. In three-fourths of the children the frequency of the attacks was lessened and in all some alleviation in severity occurred. Seventeen adults, all but two less than forty years of age, were likewise treated, but results were not as good as in young children.

Complement Titer of the Blood in Allergic Conditions. Tilden, E.: Proc. Soc. Exper. Biol. & Med. **32**: 1135, 1935.

It has been stated that the complement titer of the blood is markedly lowered in allergy. The basis of this statement did not seem sufficient. Hence, it seemed desirable to study a series of patients with hay fever and asthma. Serums from eighteen such cases were examined, as well as more than 100 controls. The titer of complement in normal blood has been found to range between 0.02 c.c. and 0.06 c.c. with an average value of 0.05 c.c. A similar titer was found for the control serums of this series, and the allergic serums also showed a similar range and similar allergic value. It is concluded that in true allergic states the average value of complement corresponds to the normal.

Sodium Chloride Tolerance in Allergic Disease. Paul, B., and Vegh, P. V.: Klin. Wchnschr. **14**: 503, 1935.

Sodium chloride tolerance tests in allergic patients reveal characteristic extensive increases in the blood chloride curve. Comparable blood chloride curves are observed in patients with impaired liver function. The similarity of curves in hepatic disease and allergic patients is considered to be further evidence for the impairment of the liver parenchyma during allergic manifestations: allergic hepatopathy.

The Source of Histamine During Anaphylaxis in Guinea Pigs. Bartosch, R.: Klin. Wchnschr. **14**: 307, 1935.

It is possible to demonstrate histamine in the fluid used for perfusion of lungs in guinea pigs which died of anaphylactic shock. Evidence is presented that this histamine is not formed, but liberated during the shock, and produces the bronchospasm after reaching the vascular system. These findings seem to suggest that anaphylactic and allergic reactions in general are due to histamine, which is liberated as a result of the antibody-antigen reaction, and which is not a product resulting from the reaction of antibody and antigen on each other.

Participation of Peripheral Nerves in Allergic Tissue Reactions. Laslowsky, J. M., and Kogan, M. M.: Arch. f. path. Anat. u. Physiol. **292**: 428, 1934.

Rabbits were sensitized subcutaneously to normal horse serum and then received an injection of horse serum into the muscles of the calf. These muscles together with the tibial and sciatic nerves were examined at intervals, as were those of non-sensitized controls which received the same dose of serum into the calf. Compared to a mild exudative reaction in the controls, the sensitized animals showed an immediate and severe inflammatory response followed by the formation of granulation tissue

and proliferation of connective tissue. The intrinsic nerve fibrils were swollen and degenerated within an hour after the injection. Such participation of nerve fibrils may explain the loss of sensation noted in allergic reactions of the skin and may be a factor in the development and course of allergic inflammation.

I. Quadermi dell' Allergia, Volume one, Number one.

This periodical, published in Milan, the first abroad devoted solely to the subject of allergy, contains three original articles submitted from clinics in Leiden and Milan, selected abstracts, and a book review.

Book Review

THE COMPLEAT PEDIATRICIAN. By WILBURT C. DAVISON, Durham, N. C., 1934, Duke University Press.

This compendium on diseases of children is a veritable almanac containing an enormous number of facts in the least possible space. In the preface, the hope is expressed that this book may serve as a "ready reminder" to be carried, like a stethoscope, in a physician's pocket or bag. An introduction contains instructions for using the book. Each symptom and sign and each disease has correlative numbers which form a system of cross reference. Innumerable tables condense essential facts. The significance of each symptom and sign, the diagnosis and treatment of each disease, preventive measures, methods of feeding, lists of drugs and prescriptions, and descriptions of laboratory methods complete this storehouse of information. It represents an enormous amount of work and detail, and as a handbook is most complete. For those interested in pediatrics, particularly medical students, internes and practitioners, this book should be most useful, once one has become accustomed to it. The subject of allergy, condensed, is well covered.